

Fig. 1A DNA and Amino Acid Sequence of Variable Region of FR1-H7 Heavy Chain

Heavy chain variable region sequence (cDNA)

```
ATGGCCGAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGG  
GCCTCAGTGAAGGTTCTGCAAGGTTCTGGATAACACCTCACCGACTACTA  
CATGCACTGGGTGCAACAGGCCCTGGAAAAGGGCTTGAGTGGATGGGACTT  
GTTGATCCTGAAGATGGTAAACAATCTACGCAGAGAAGTTCCAGGGCAGAG  
TCACCATAACCGCGGACACGTCTACAGACACAGCCTACATGGAGCTGAGCAG  
CCTGAGATCTGAGGACACGCCGTATTACTGTGCGAGAGATGACTACATG  
GACGTCTGGGGCAAAGGCACCCCTGGTACCGTCTCAAGCGCCTCCACCAAGG  
GCCCA
```

Heavy chain variable region sequence (amino acid)

```
MAEVQLVQSGAEVKPGASVKVSCKVSGYTFTDYYMHWVQQAPGKGLEWMG  
LVDPEDGETIYAEKFQGRVTITADTSTDAYMELSSLRSEDTAVYYCARDDYMD  
VWGKGTLTVSSASTKGP
```

Fig. 1B DNA and Amino Acid Sequence of Variable Region of FR1-H7 light Chain**Light chain variable region sequence (cDNA)**

CTTGAAACGACACTCACGCAGTCTCCAGACACCCTGTCTTGTCTCCAGGAGA
AGGAGCCACCCTTCCTGTAGGGCCAGTCAGAGTGTAGCGGCAGTGCCTTG
GCCTGGTACCAGCAGAACCTGGCCAGGCTCCAGACTCCTCATCTATGATG
CATCCAGTAGGGCCACTGGCGTCCCAGACAGGTTAGTGGCAGTGGGTCTGG
GGCAGACTTCAGTCTCACCATCAGCAGACTGGAGCCTGAAGATTTCAGTG
TATTCCTGTCAGCAATATGGTAGCTCACCTCTCACTTCGGCCCTGGGACCAA
AGTGGATGTCAAACGAACGTGGCTGCACCATCTGTCTTCATCTCCGCCAT
CTGATGAGCAGTTGAAACTGGAACTGCCTCTGTTGTGCCTGCTGAATAAC
TTCTATCCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATT

Light chain variable region sequence (amino acid)

LETTLTQSPDTLSLSPGEGATLSCRASQSVSGSALAWYQQKPGQAPRLLIYDASS
RATGVPDRFSGSGADFSLTISRLEPEDFAVYSCQQYGSSPLFGPGTKVDVKR
TVAAAPSVFIFPPSDEQLKSGTASVVCLNNFYPREAKVQWKVD

Fig. 1C CDRs For FR1-H7 Nucleic Acid Sequences**VH (human heavy chain subclass I)**

CDR1 GACTACTACATGCAC
CDR2 CTTGTTGATCCTGAAGATGGTGAAACAATCTACGCAGAGAAGTTCCAGGGC
CDR3 GATGACTACATGGACGTC

VL (human kappa light chain subgroup III)

CDR1 AGGGCCAGTCAGAGTGTAGCGGCAGTGCCTGGCC
CDR2 GATGCATCCAGTAGGGCCACT
CDR3 CAGCAATATGGTAGCTCACCTCTCACT

Fig. 1D CDRs For FR1-H7 Amino Acid Sequences**VH (human heavy chain subclass I)**

CDR1 DYYMH
CDR2 LVDPEDGETIYAEKFQG
CDR3 DDYMDV

VL (human kappa light chain subgroup III)

CDR1 RASQSVSGSALA
CDR2 DASSRAT
 CDR3 QQYGSSPLT

Fig. 2A DNA and Amino Acid Sequence of Variable Region of FR1-A1 Heavy Chain

Heavy chain variable region sequence (cDNA)

```
ATGGCCCAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGT  
CCTCGGTGAAGGTCTCCTGCAAGGCTTCTGGATCGACCTTCACCGGCTACTAT  
ATGCAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTGGATGGGAAGG  
ATCATCCCTATCCTTGGTATA GCAA ACTACGCACAGAACGTTCCAGGGCAGAG  
TCACGATTACCGCGGACAAATCCACGAGCACAGCCTACATGGAGCTGAGCAG  
CCTGAGATCTGAGGACACGGCCGTGTACTACTGTGCGAGAGGAGGAGATCTG  
GGCGGTATGGACGTCTGGGGCCAAGGGA
```

Heavy chain variable region sequence (amino acid)

```
MAQVQLVQSGAEVKKPGSSVKVSCKASGQTFTGYYMHWVRQAPGQGLEWMG  
RIIPILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCARGGDLGG  
MDVWGQQG
```

Fig. 2B DNA and Amino Acid Sequence of Variable Region of FR1-A light Chain**Light chain variable region sequence (cDNA)**

**CTTGAAATTGTGCTGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGA
GCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCCTCCGGCATAGTAATGGA
TACAACATATTGGATTGGTACCTGCAGAACGCCAGGGCAGTCTCCACAGCTCCT
GATCTATTGGCTTCTAATCGGGCCTCCGGGGTCCCTGACAGGTTAGTGGCA
GTGGATCAGGCACAGATTACACTGAAAAATCAGCAGAGTGGAGGCTGAGGA
TGTGGGGTTTATTACTGCATGCAAGCTCTACAAATTCCCTCCGACTTCGGCC
CTGGGACCAAAGTGGATATCAAACGAACGTGGCTGCA**

Light chain variable region sequence (amino acid)

**LEIVLTQSPLSLPVTPGE~~PASISCRSSQSLRHSNG~~NYLDWYLQKPGQSPQLLIYL
ASN~~RASGPDRFSGSG~~TDFTLKISRVEAEDVGVYYCMQALQIPPTFGPGTKVD
IKRTVAA**

Fig. 2C CDRs For FR1-A1 Nucleic Acid Sequences**VH (human heavy chain subclass I)**

CDR1 GGCTACTATATGCAC
CDR2 AGGATCATCCCTATCCTTGGTATAGCAAAC TACGCACAGAAGTTCCAGGGC
CDR3 GGAGGAGATCTGGCGGTATGGACGTC

VL (human kappa light chain subgroup II)

CDR1 AGGTCTAGTCAGAGCCTCCGGCATAGTAATGGATAACAAC TATTGGAT
CDR2 TTGGCTTCTAACCGGGCTCC
CDR3 ATGCAAGCTCTACAAATTCCCTCCGACT

Fig. 2D CDRs For FR1-A1 Amino Acid Sequences**VH (human heavy chain subclass I)**

CDR1	GYYMH
CDR2	RIIPILGIANYAQKFQG
CDR3	GGDLGGMDV

VL (human kappa light chain subgroup II)

CDR1	RSSQSLRHNSNGNYLD
CDR2	LASNKRAS
CDR3	MQALQIPPT

Fig. 3

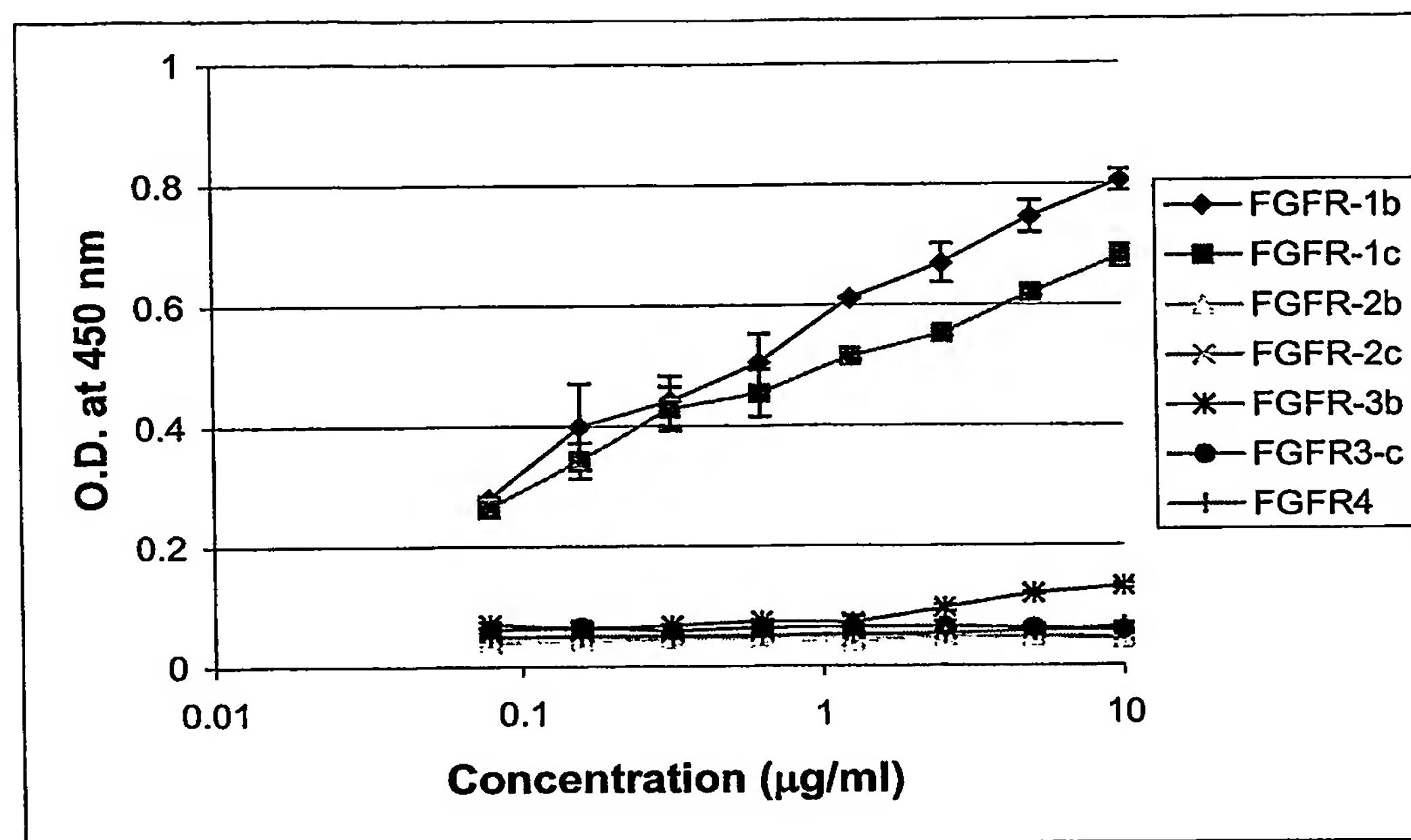


Fig. 4A

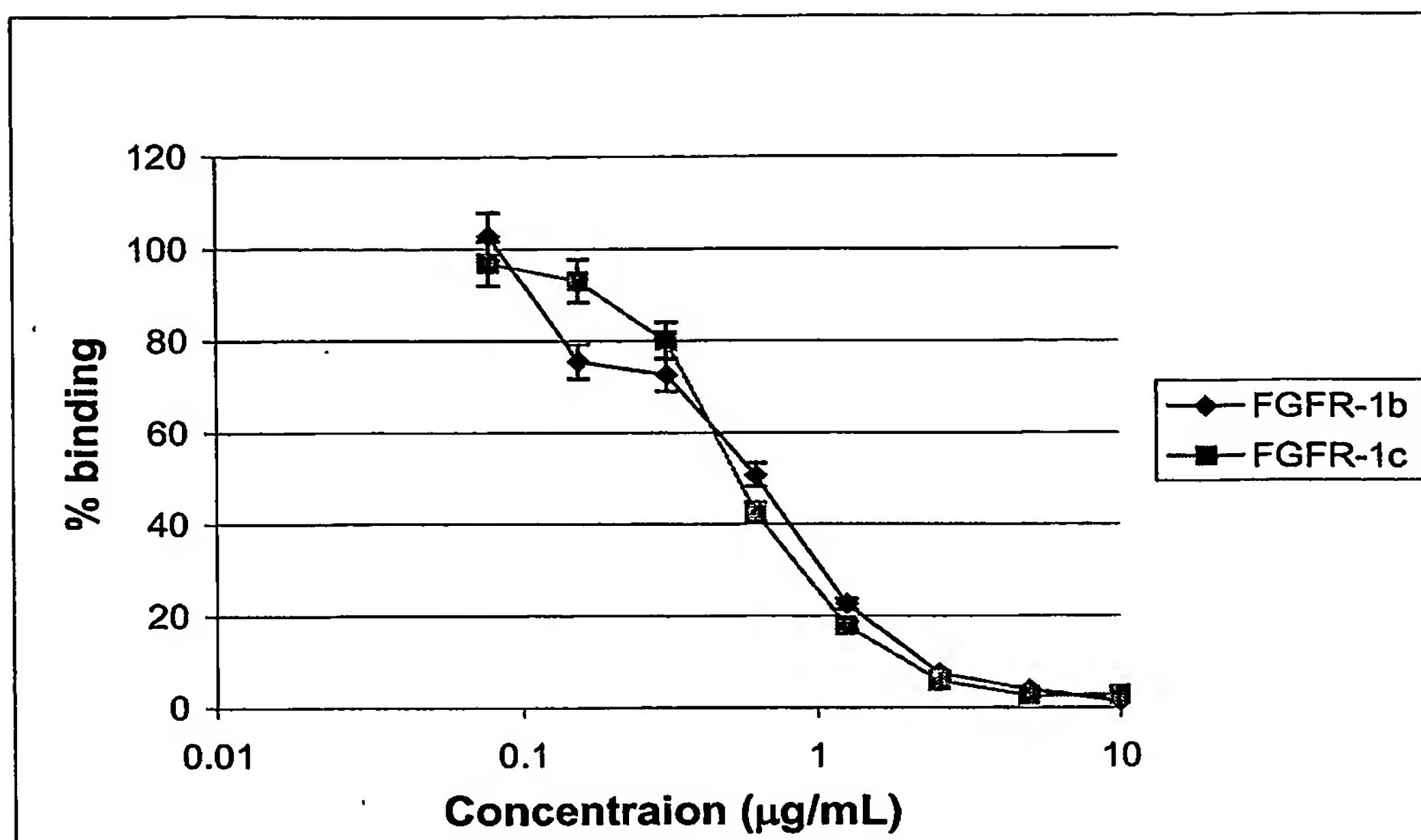


Fig. 4B

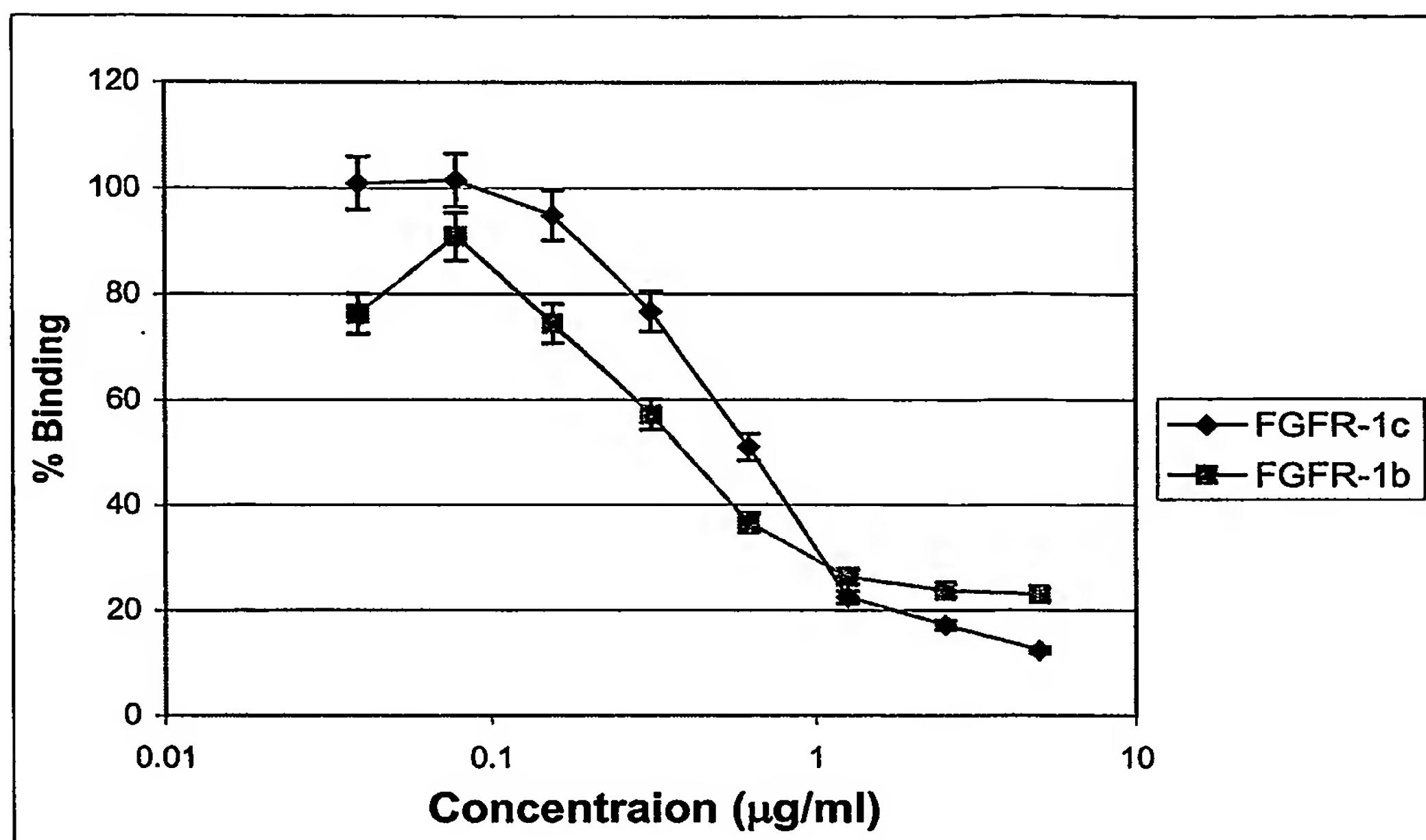


Fig. 5A

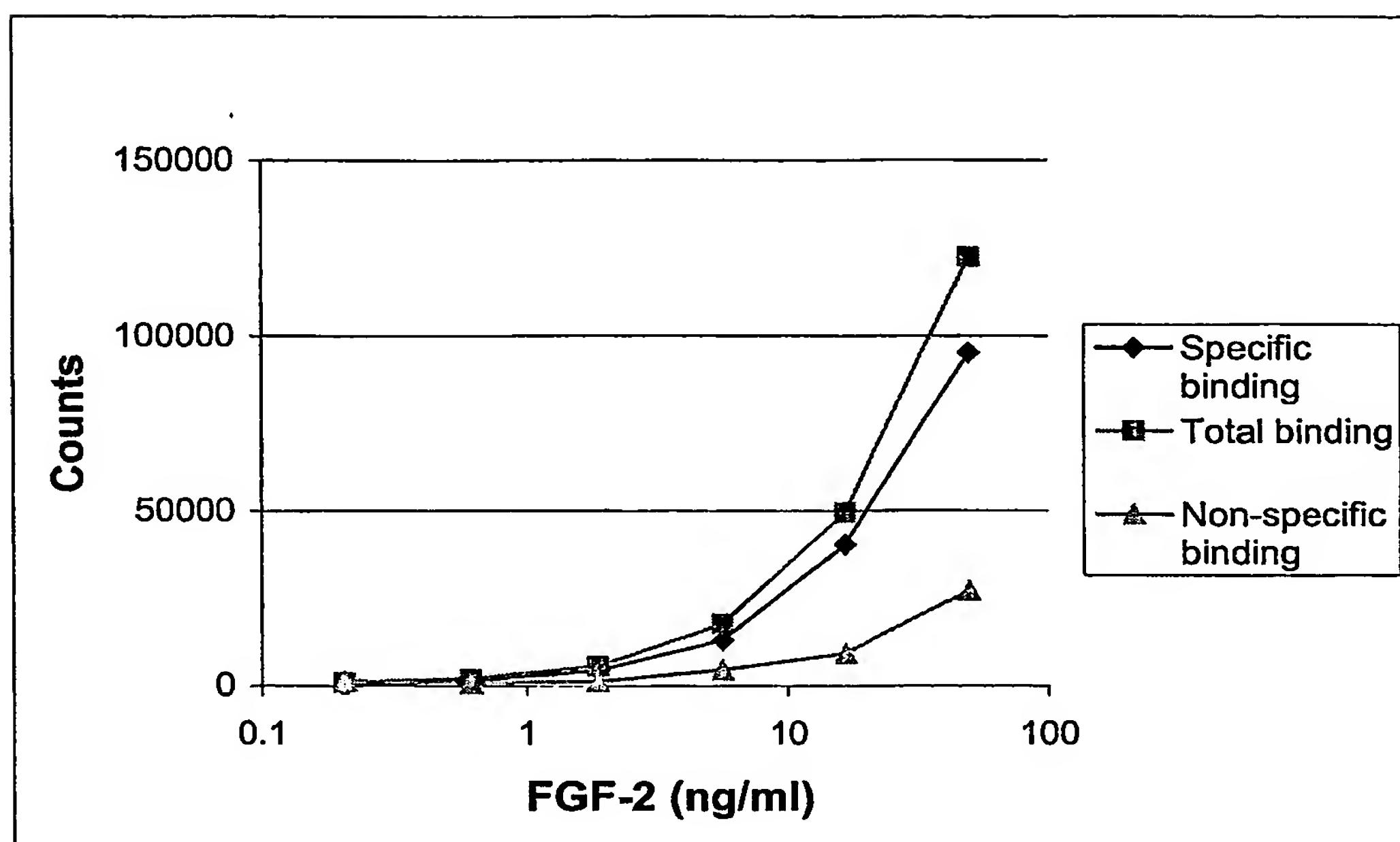


Fig. 5B

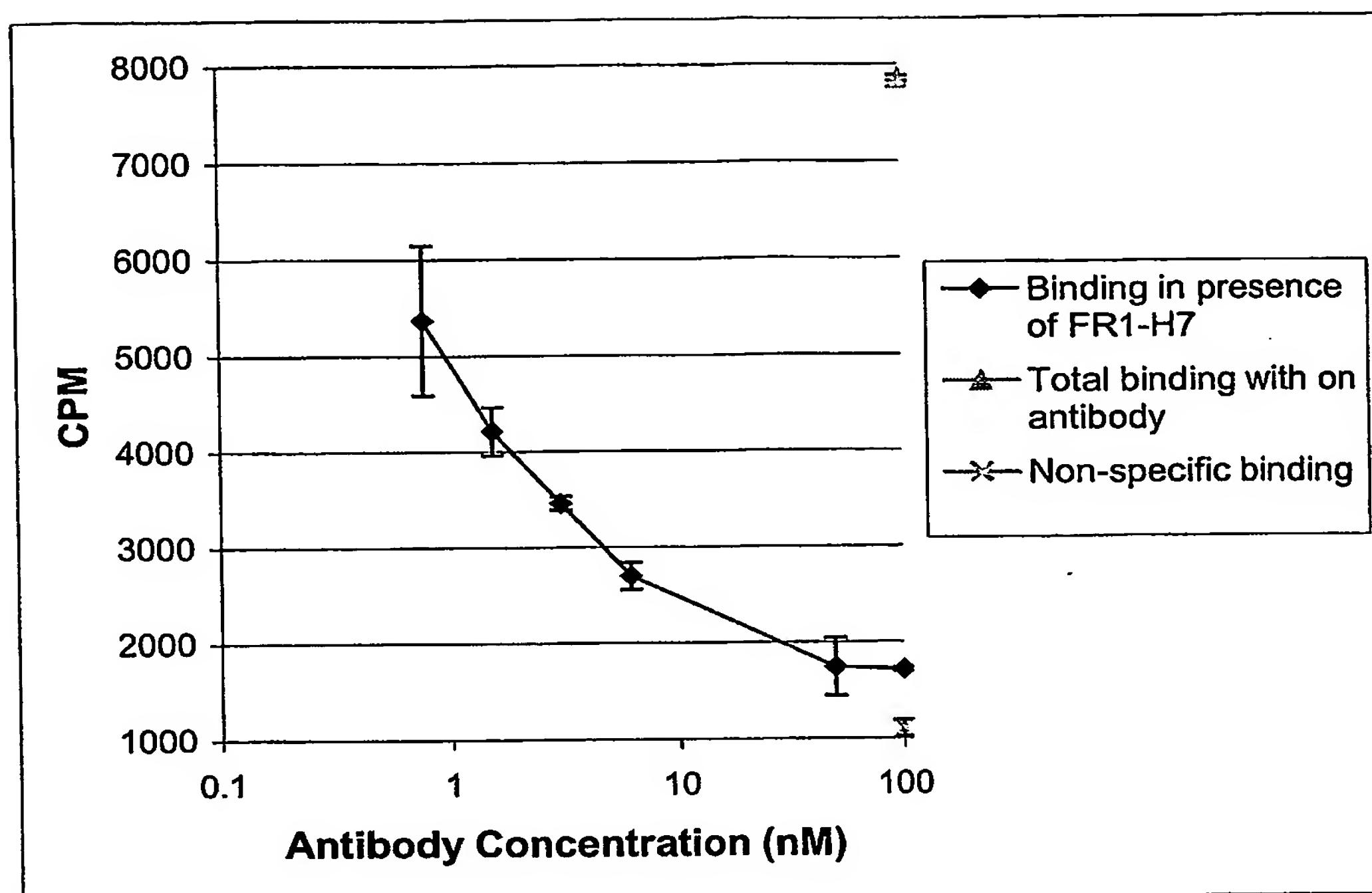


Fig. 6

FGF-2 (ng/ml)	-	20	20	-
FR1-H7 (μg/ml)	-	30	-	30
Molecular weight marker				

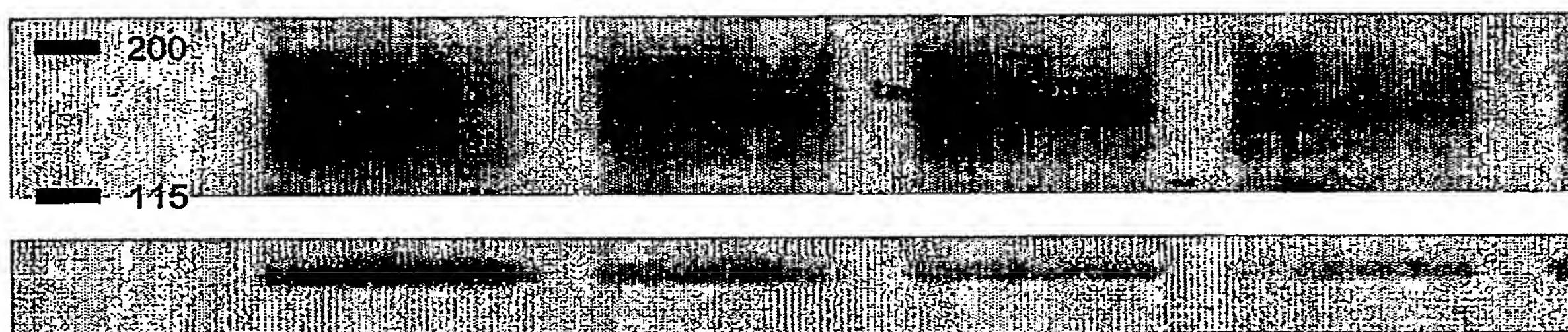


Fig. 7

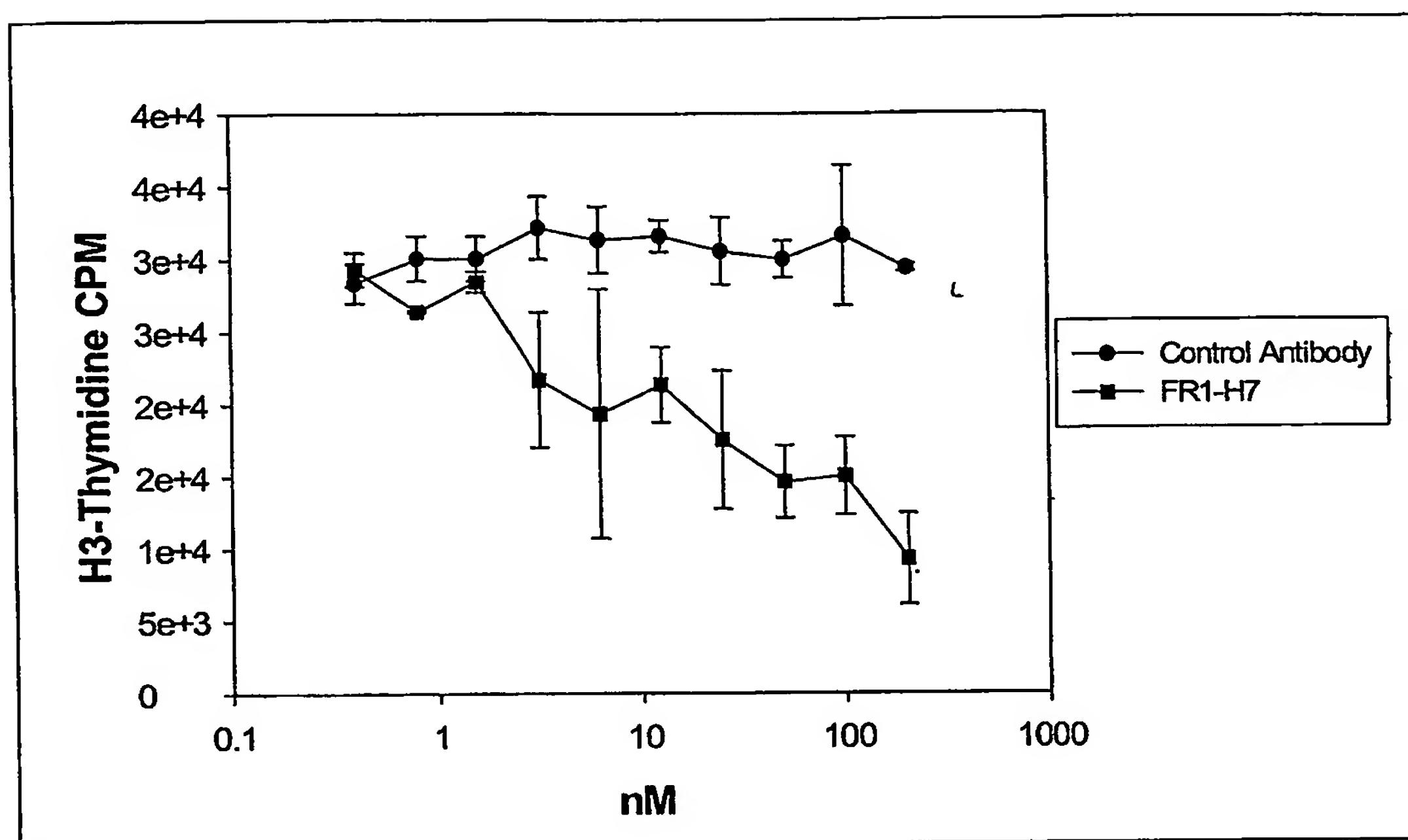


Fig. 8A

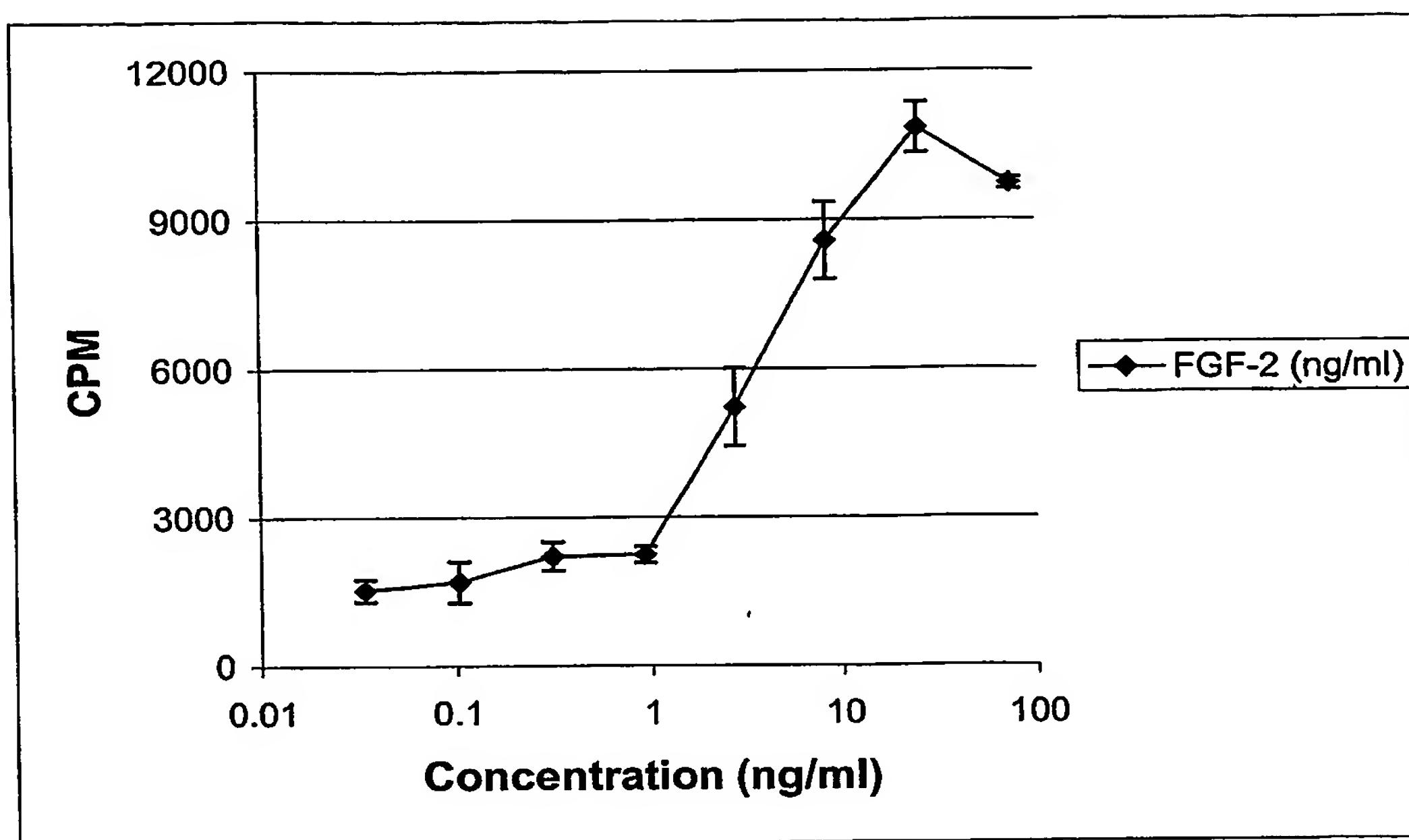


Fig. 8B

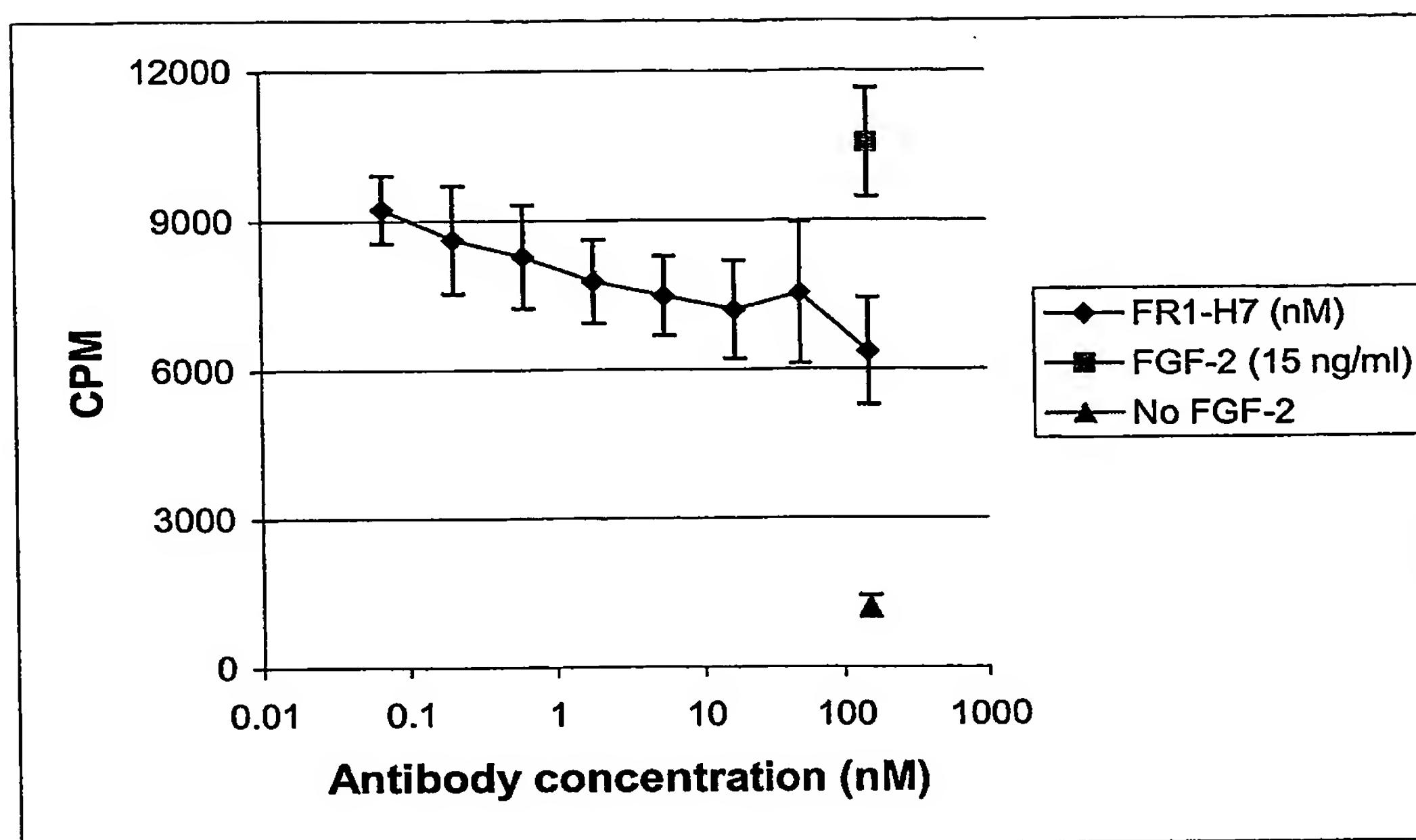
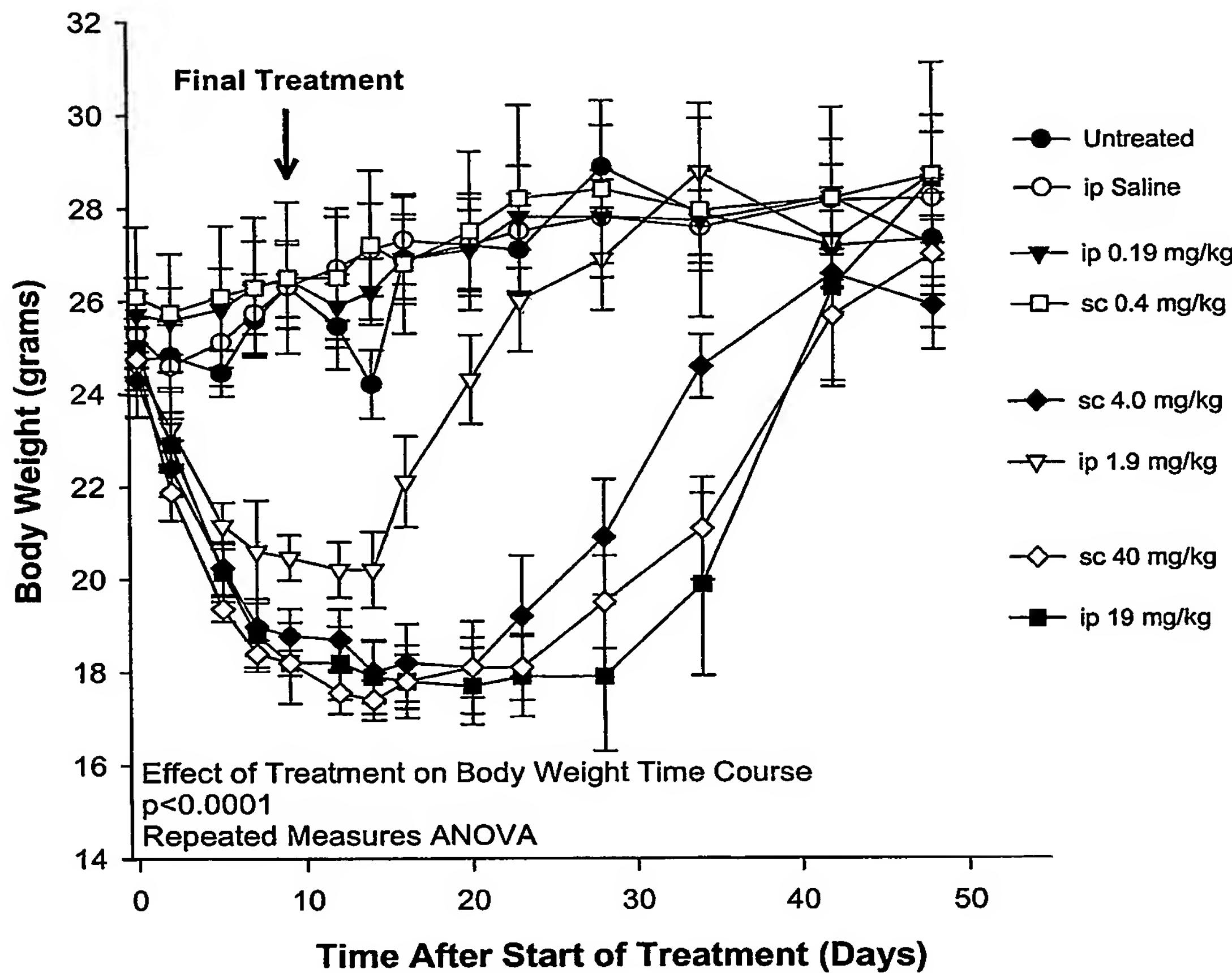


Fig. 9



*13 gram mouse euthanized

Fig. 10

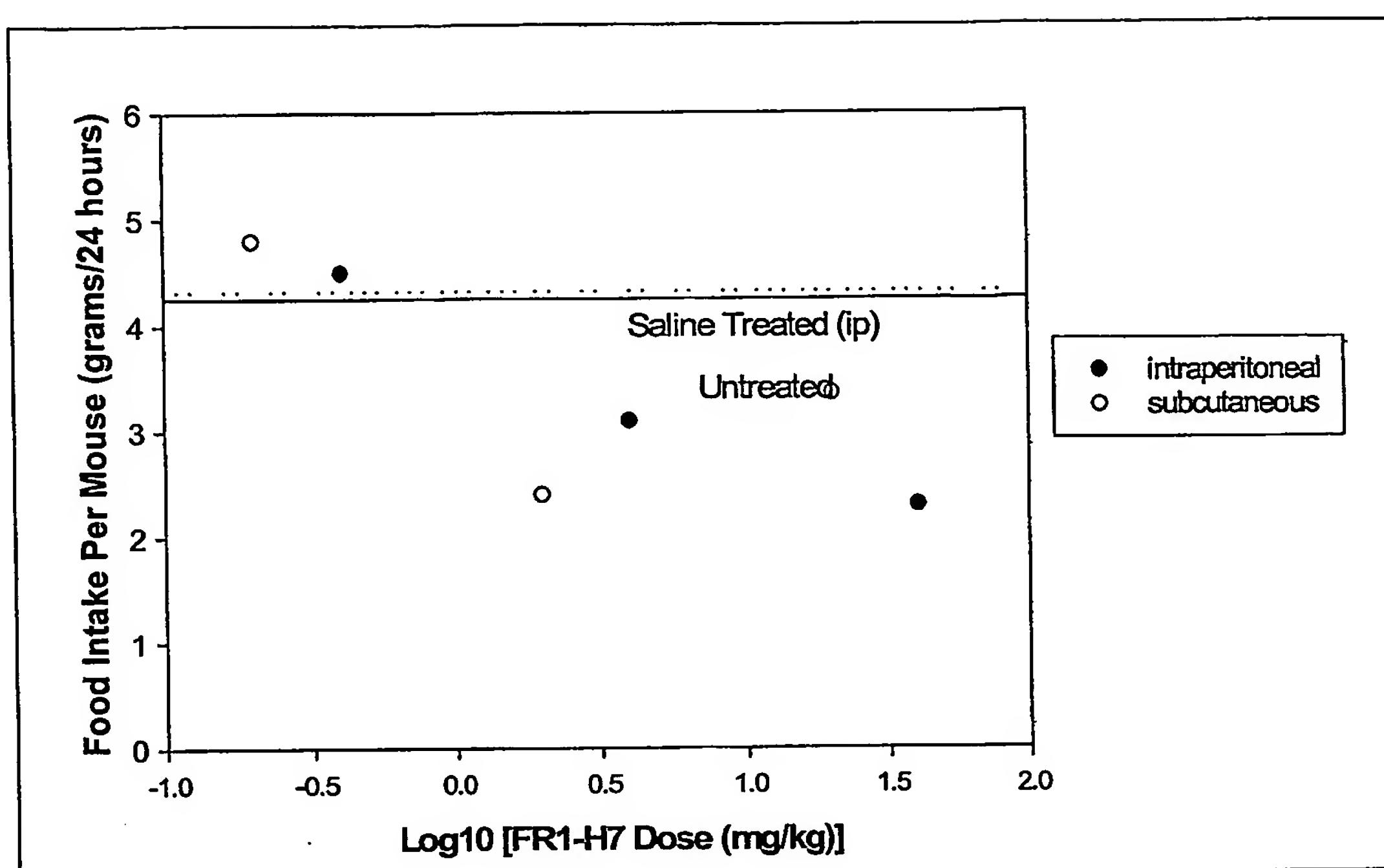


Fig. 11

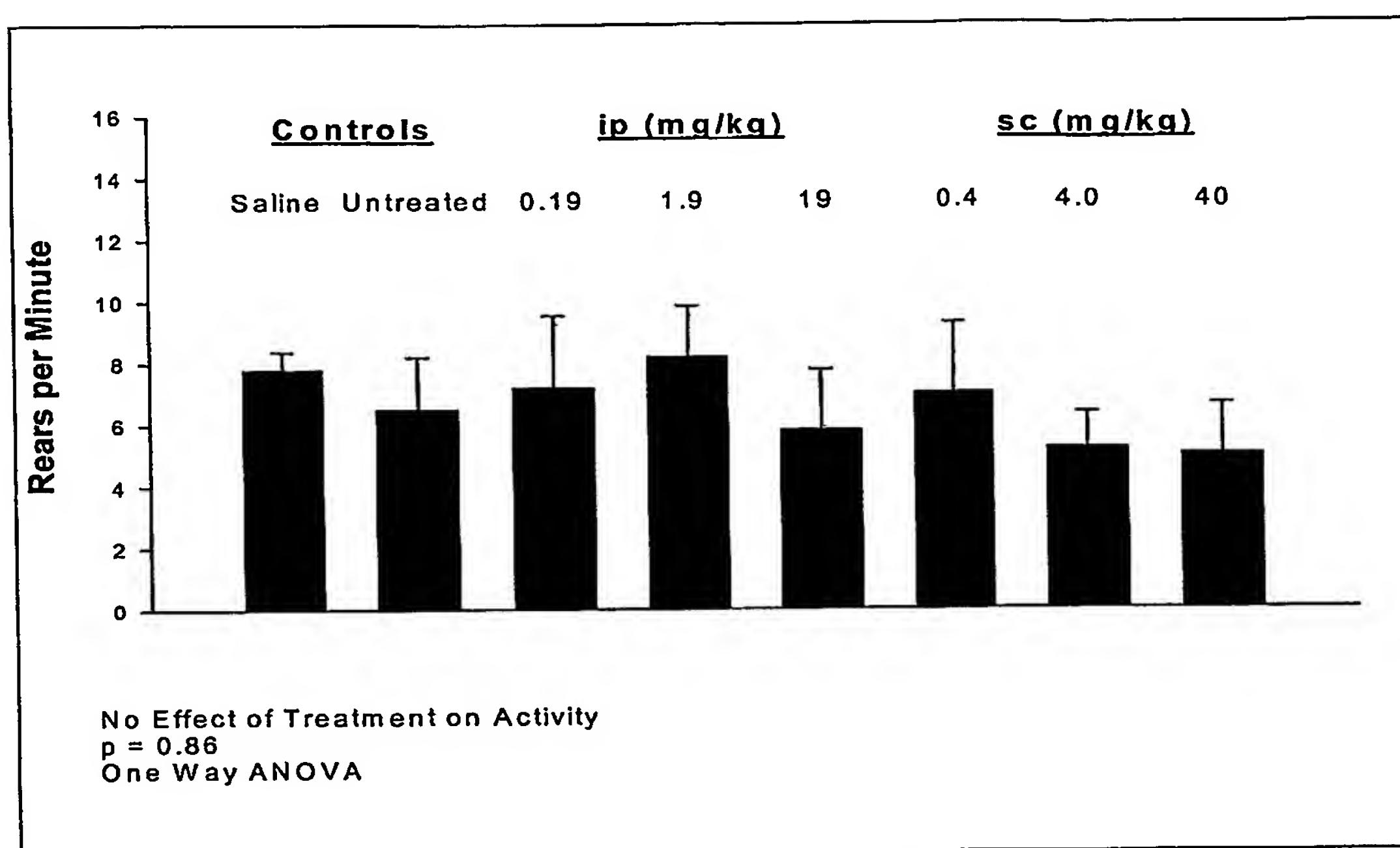


Fig. 12A

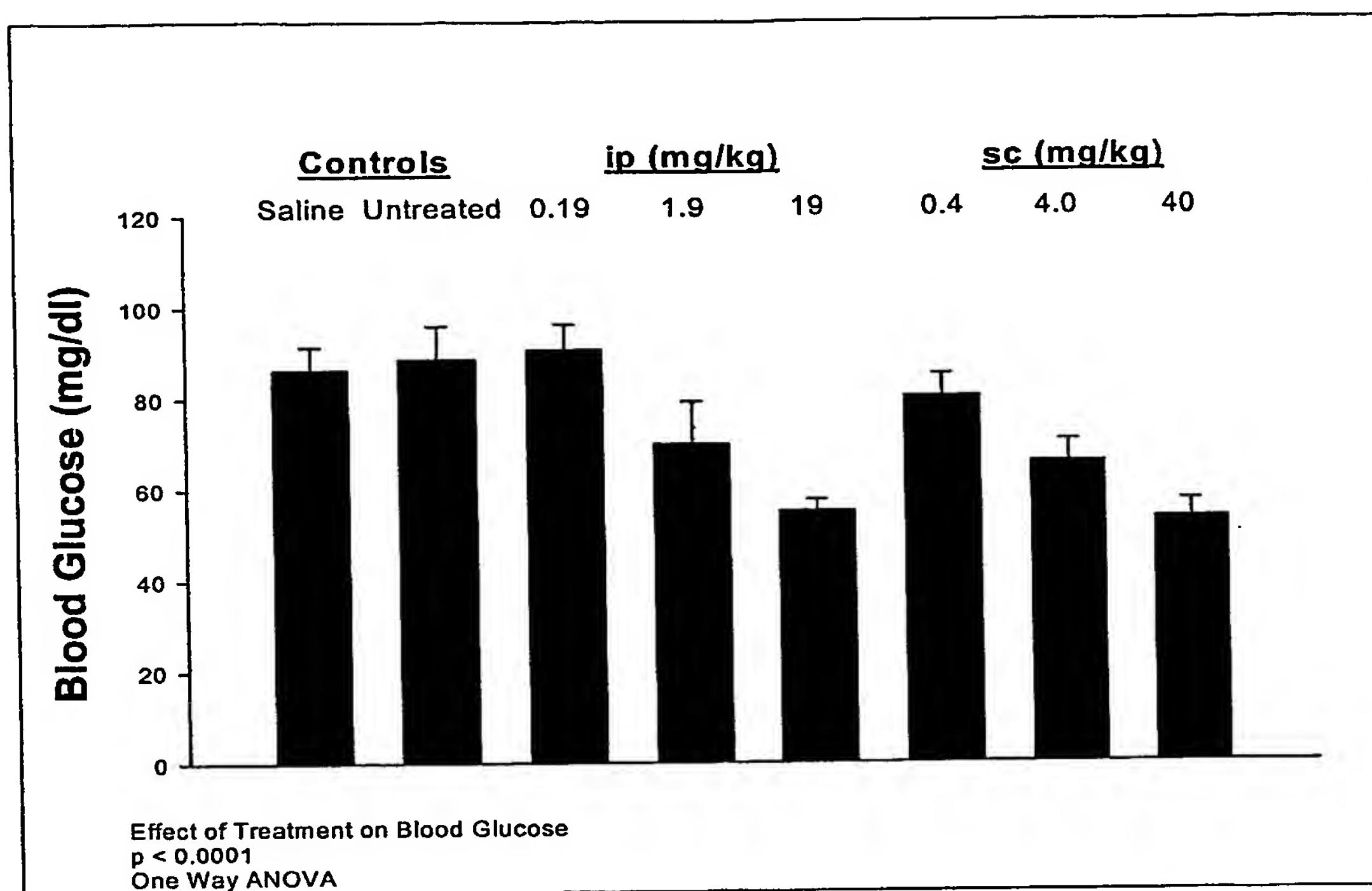


Fig. 12B

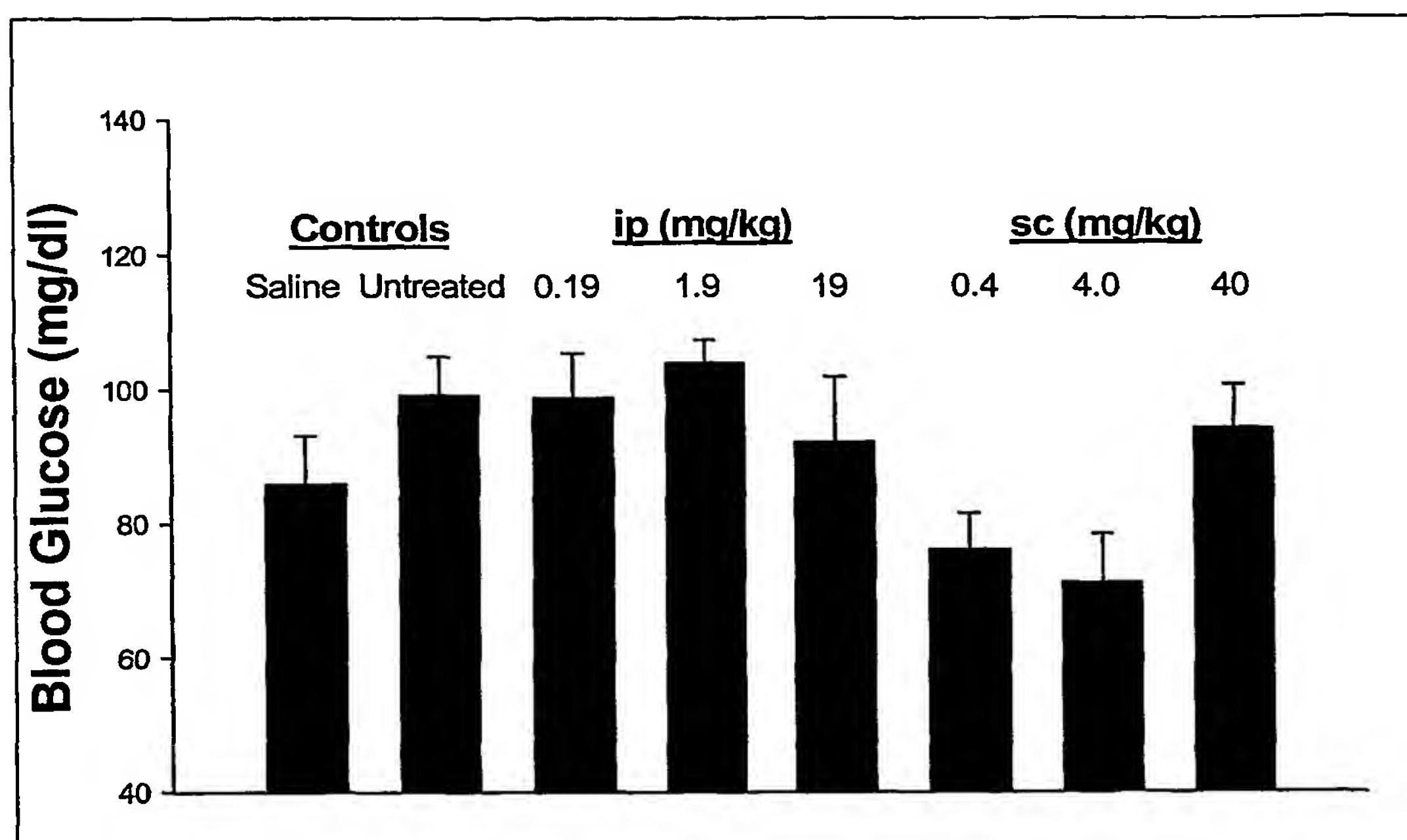


Fig. 13

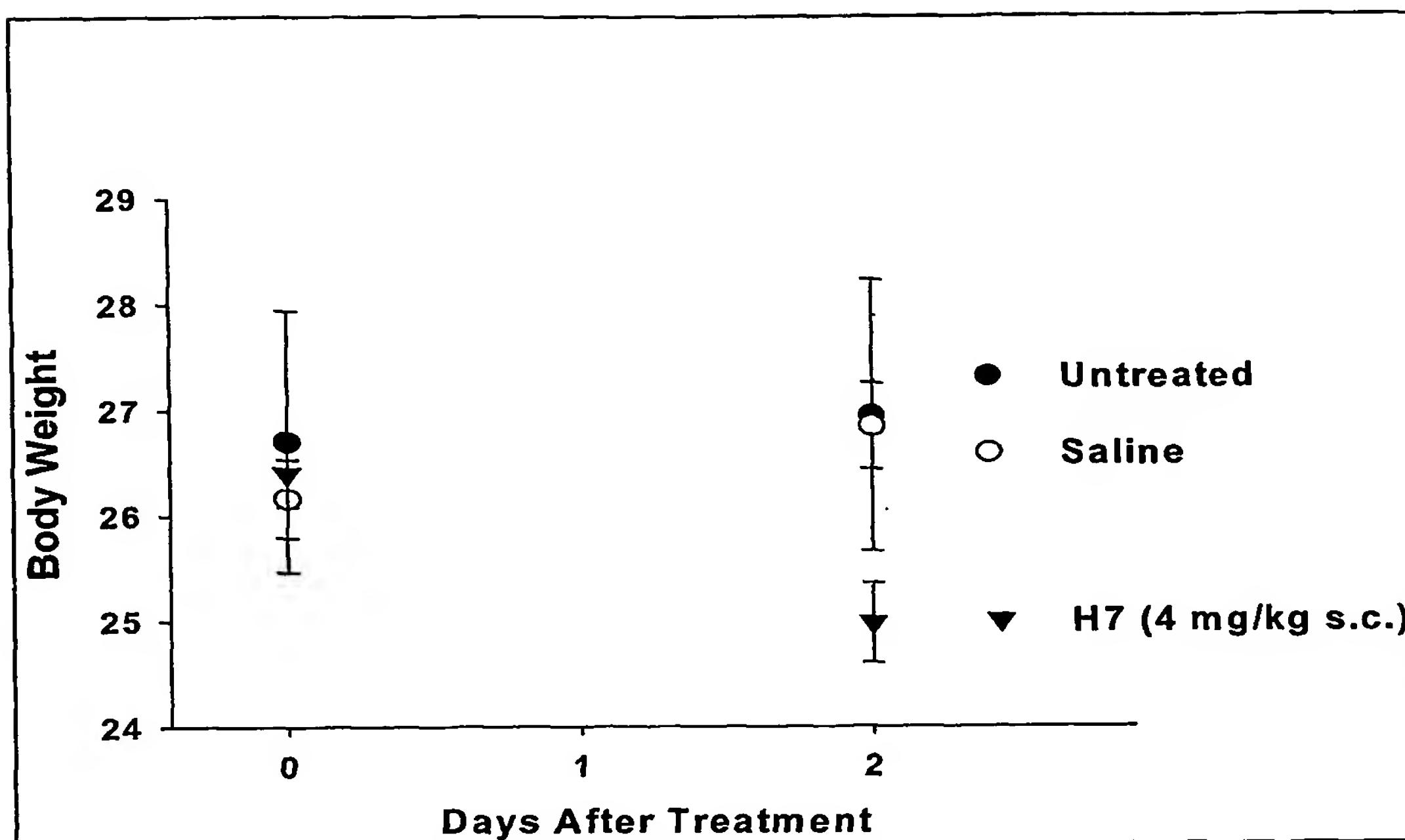
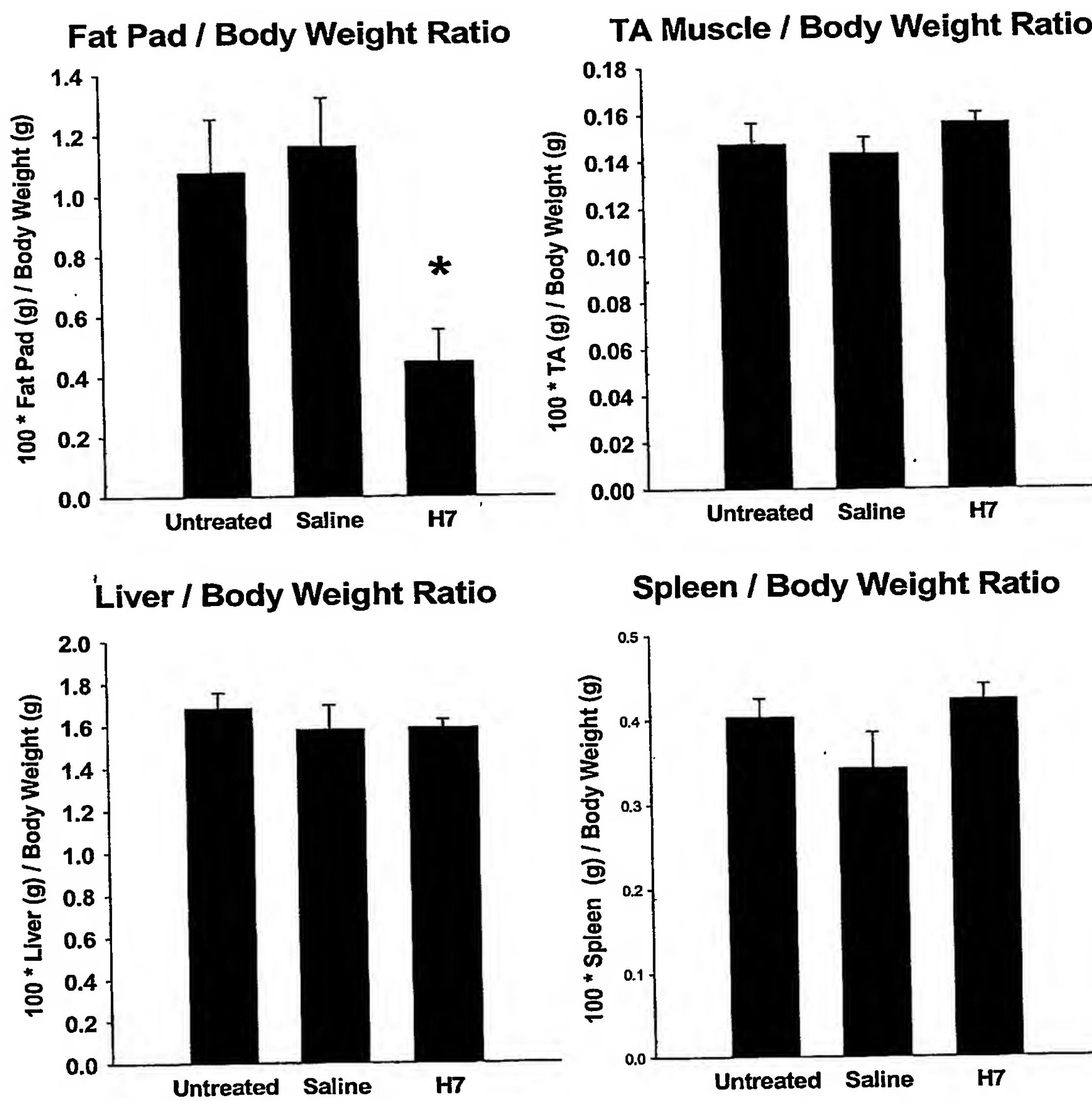


Fig. 14



*
p<0.05

Fig. 15A

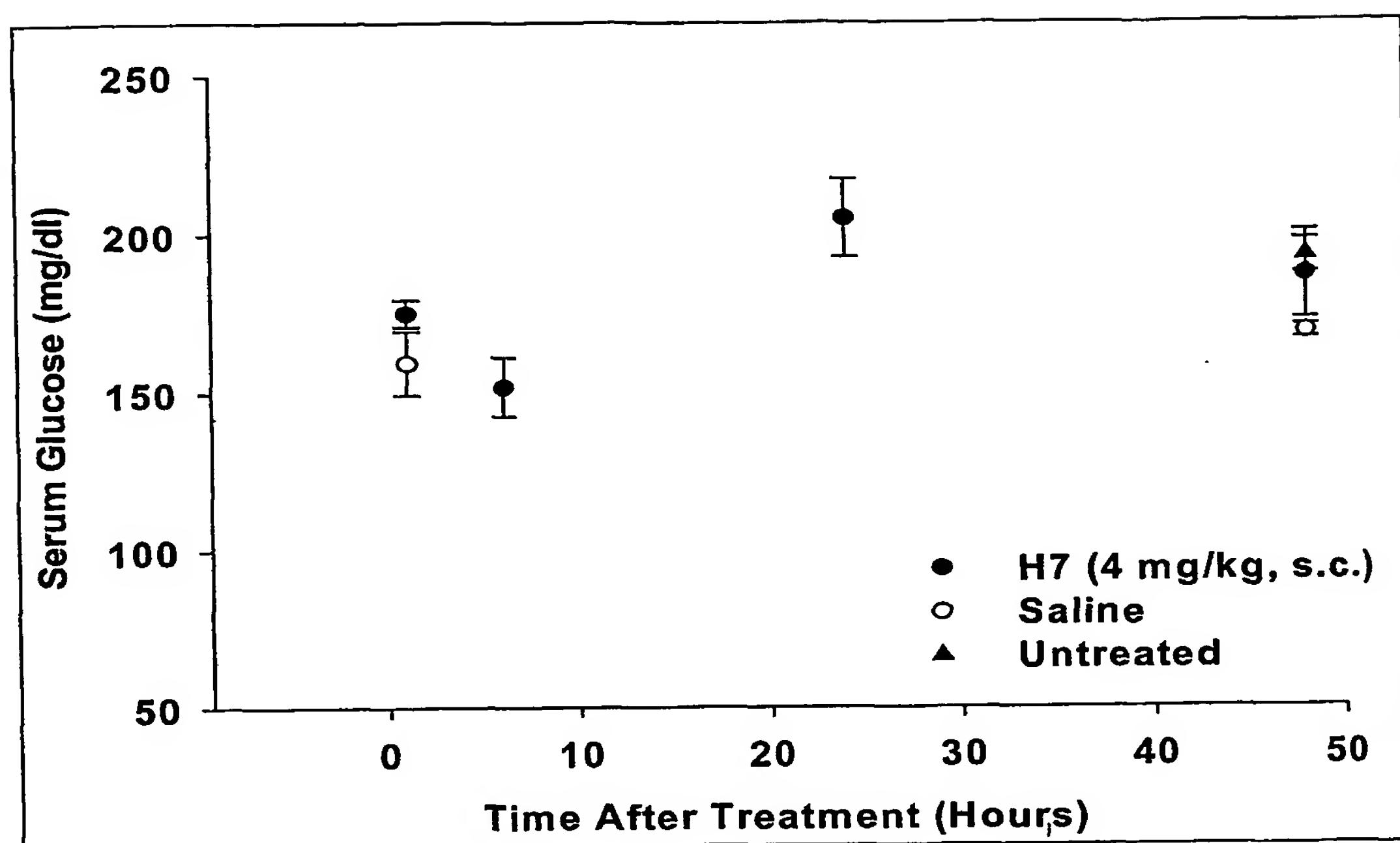


Fig. 15B

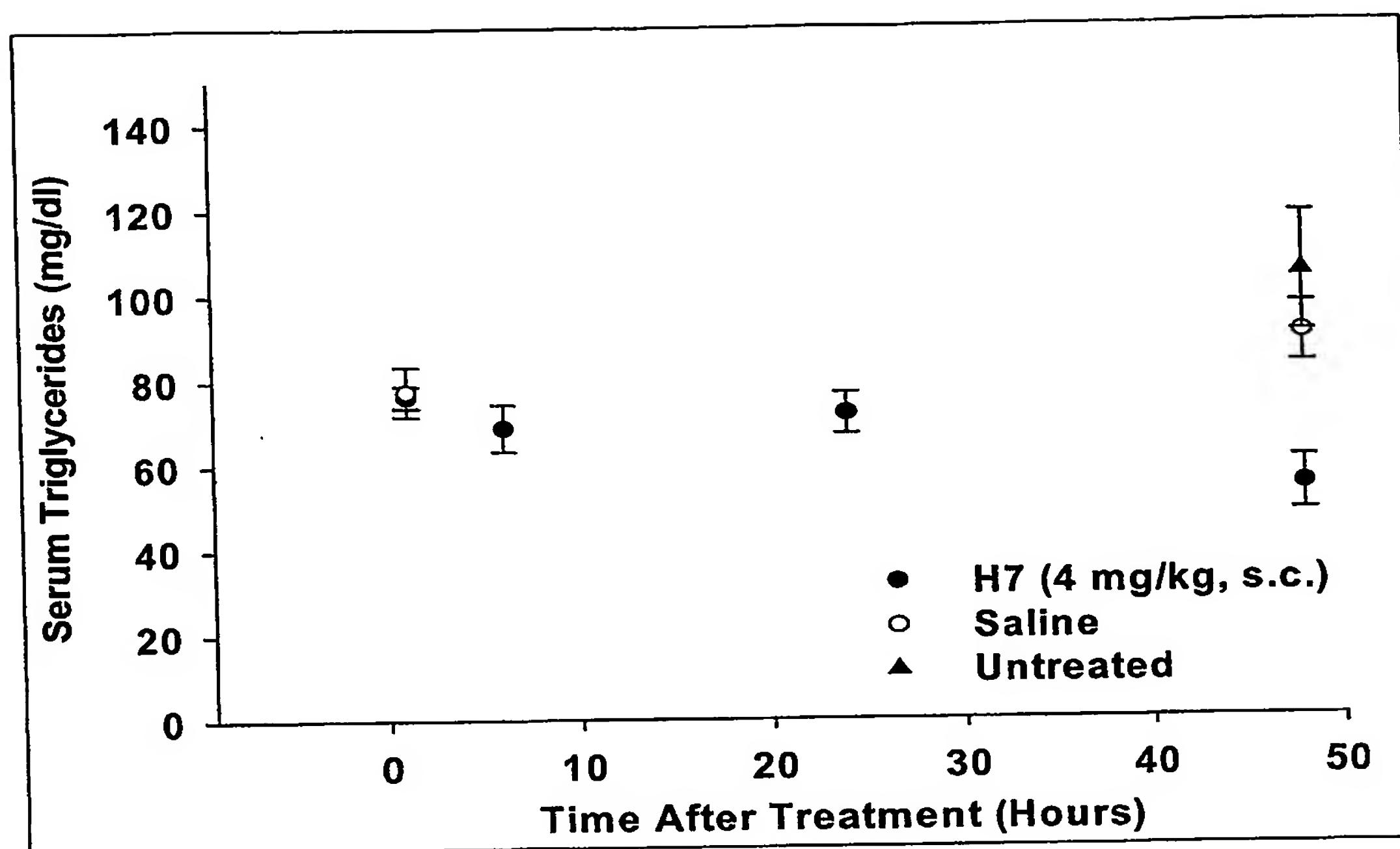


Fig. 15C

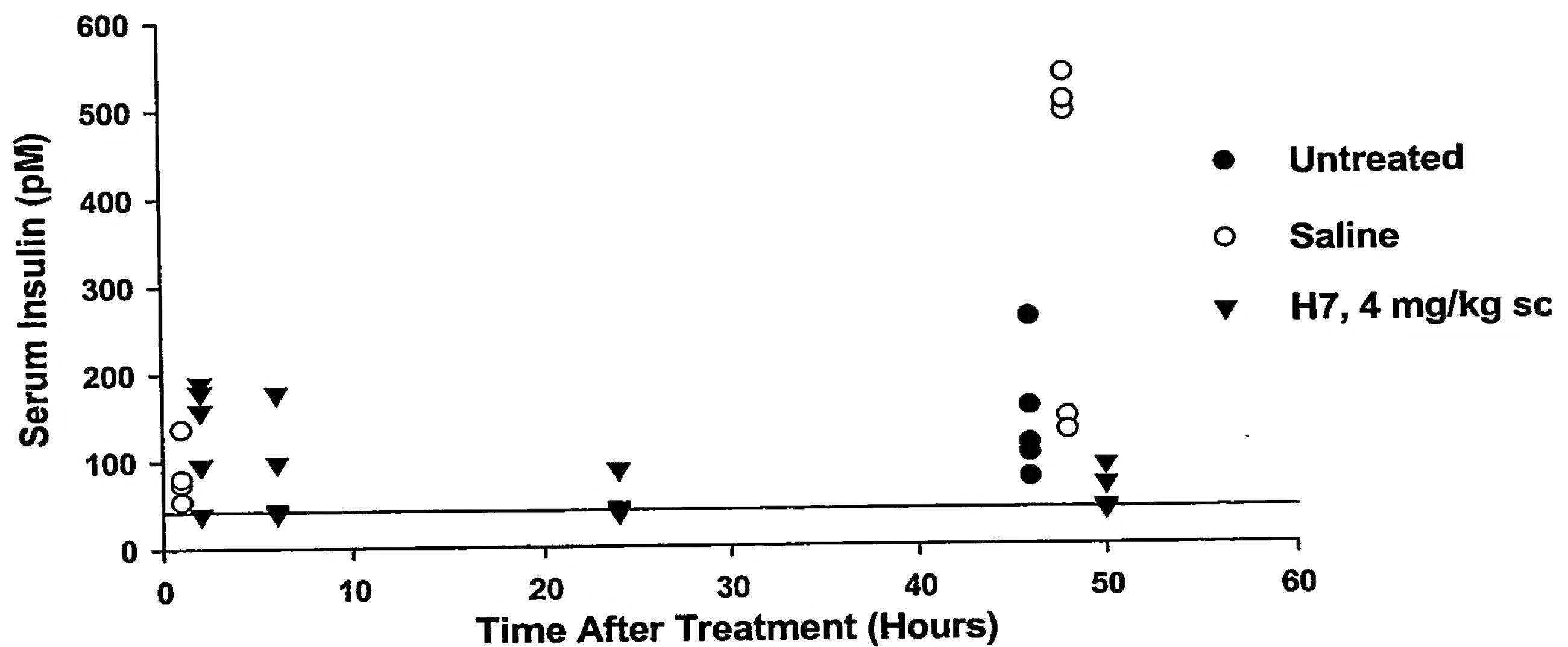


Fig. 15D

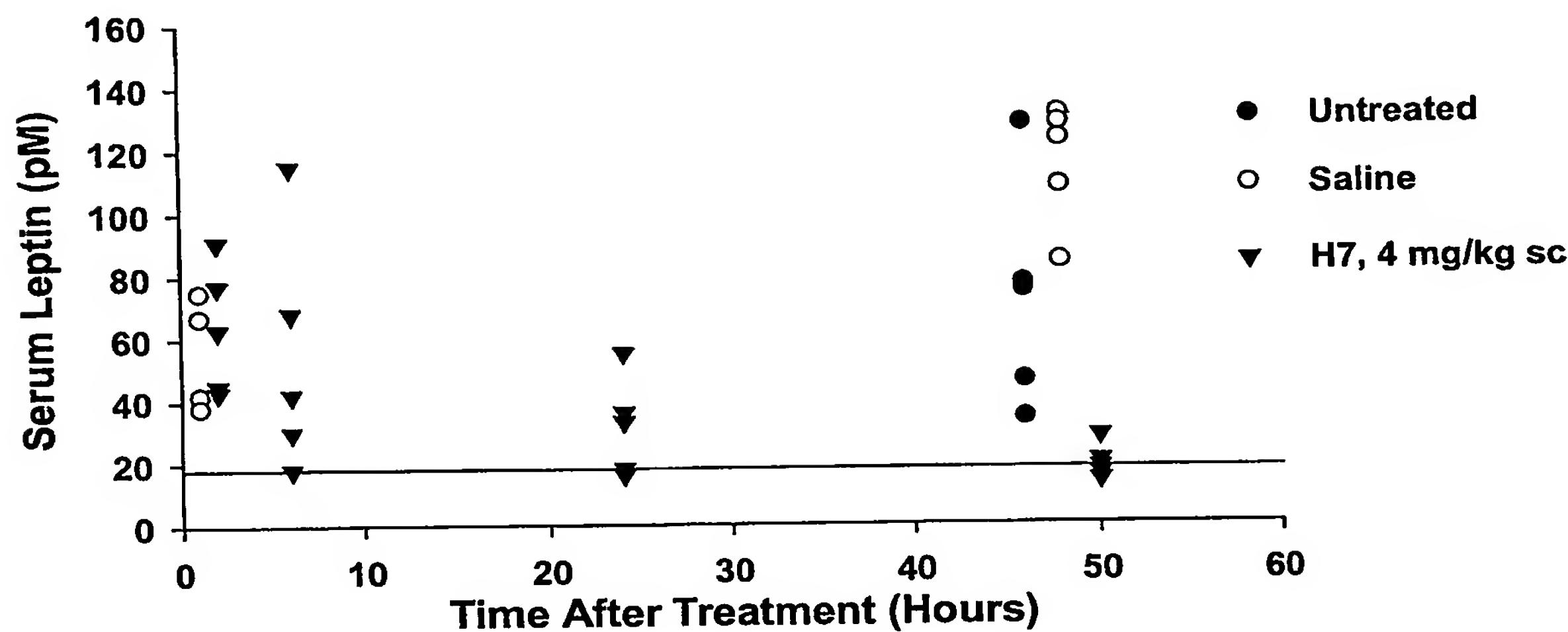


Fig. 16

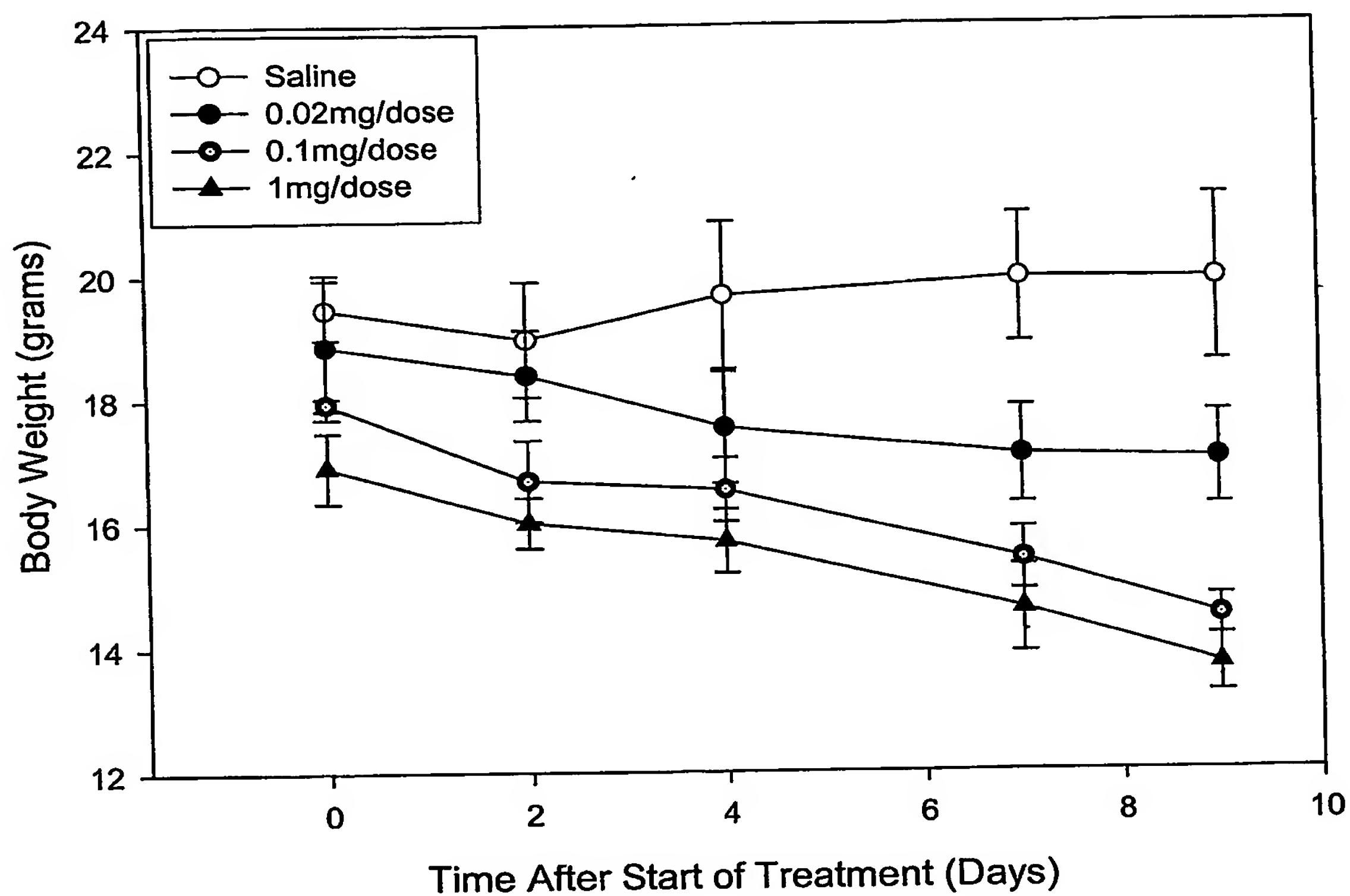


Fig. 17

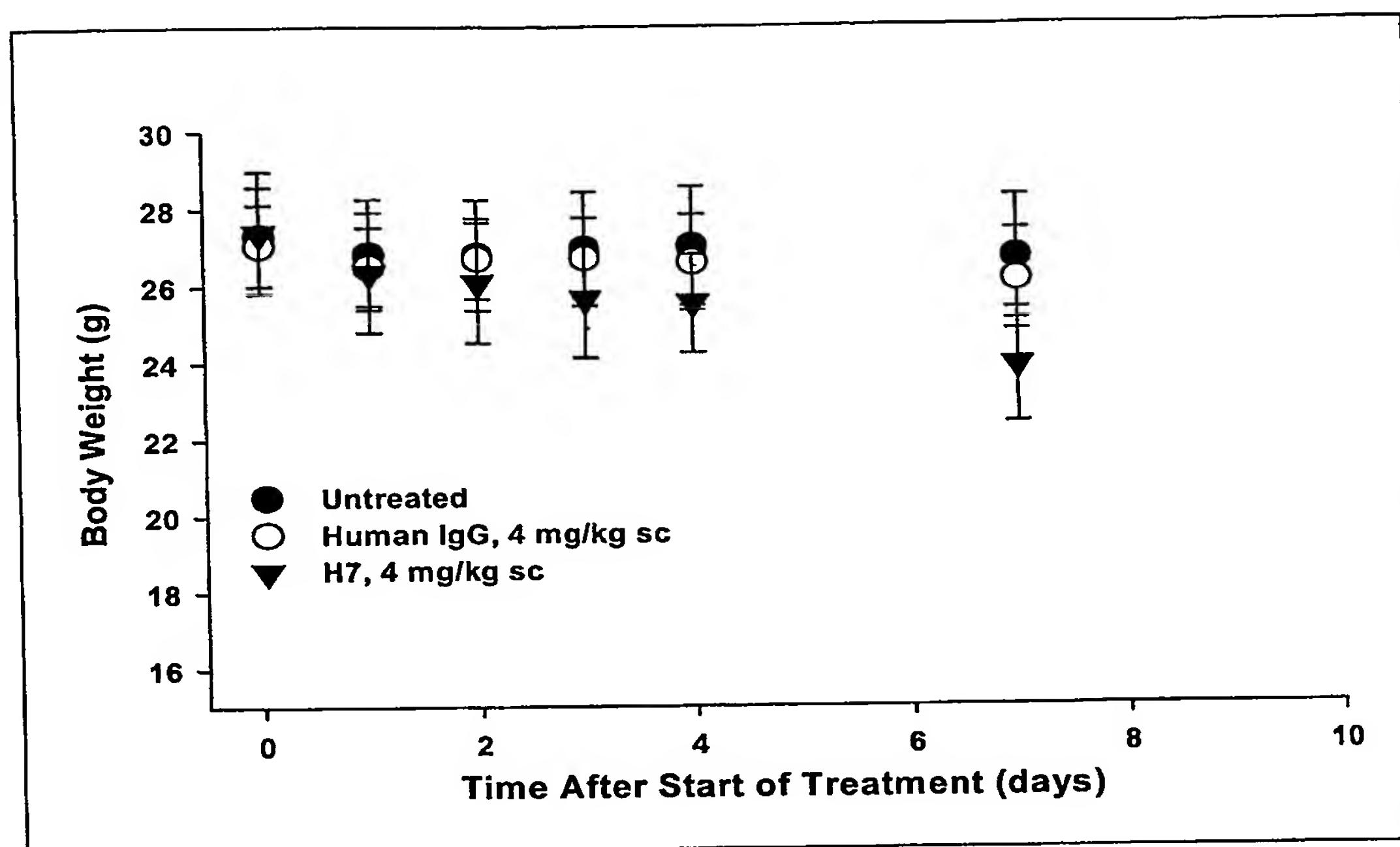


Fig. 18

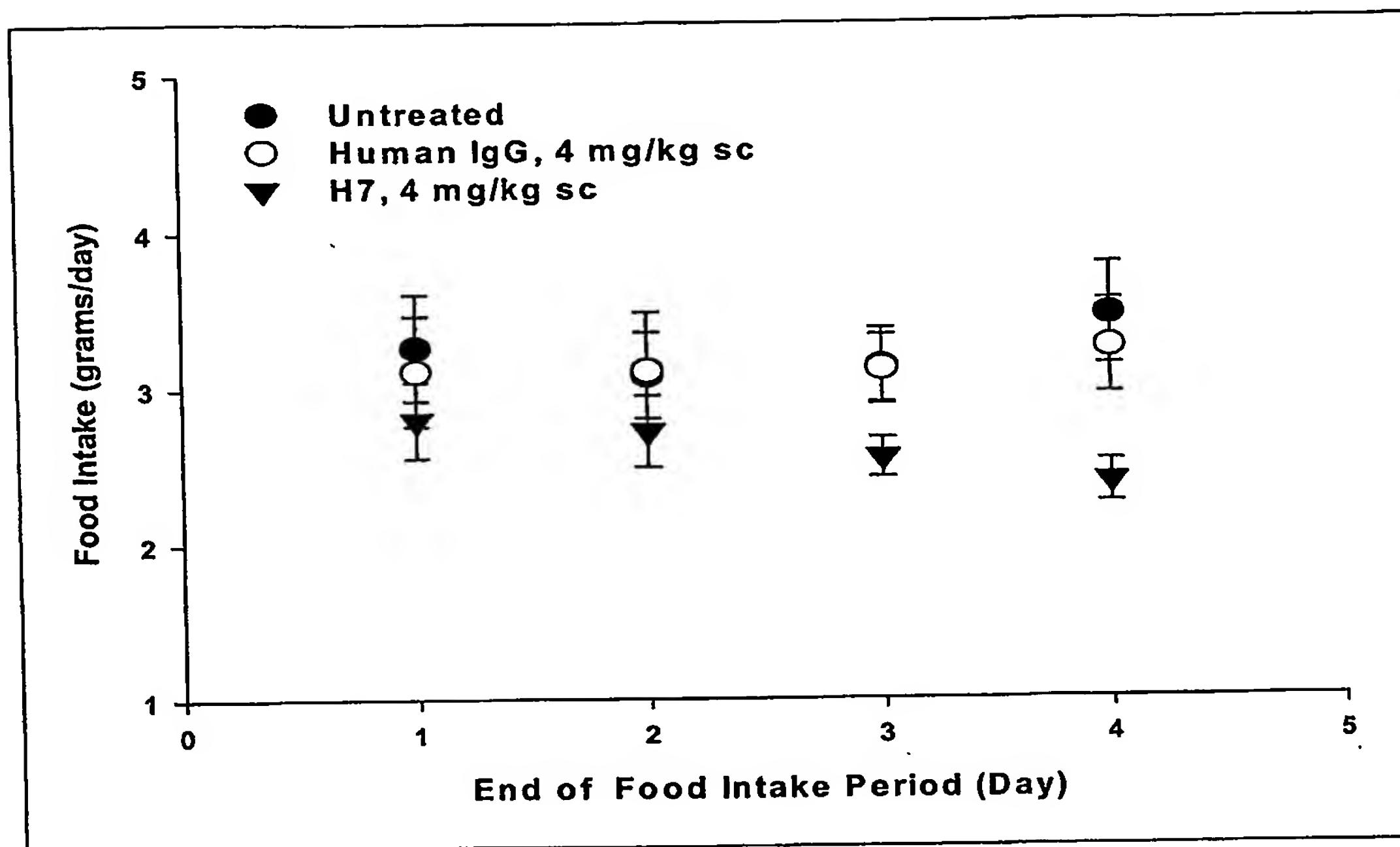


Fig. 19

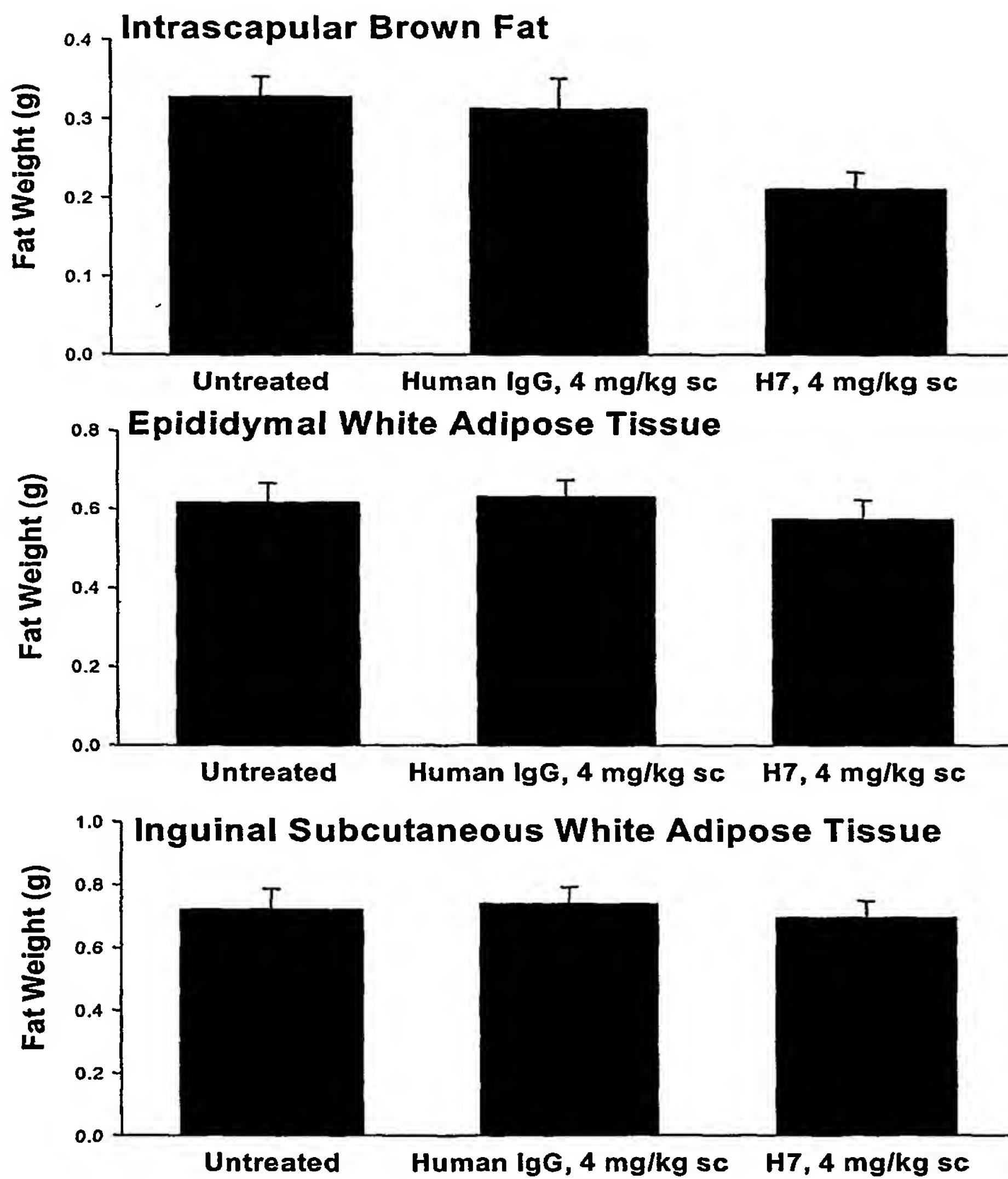


Fig. 20

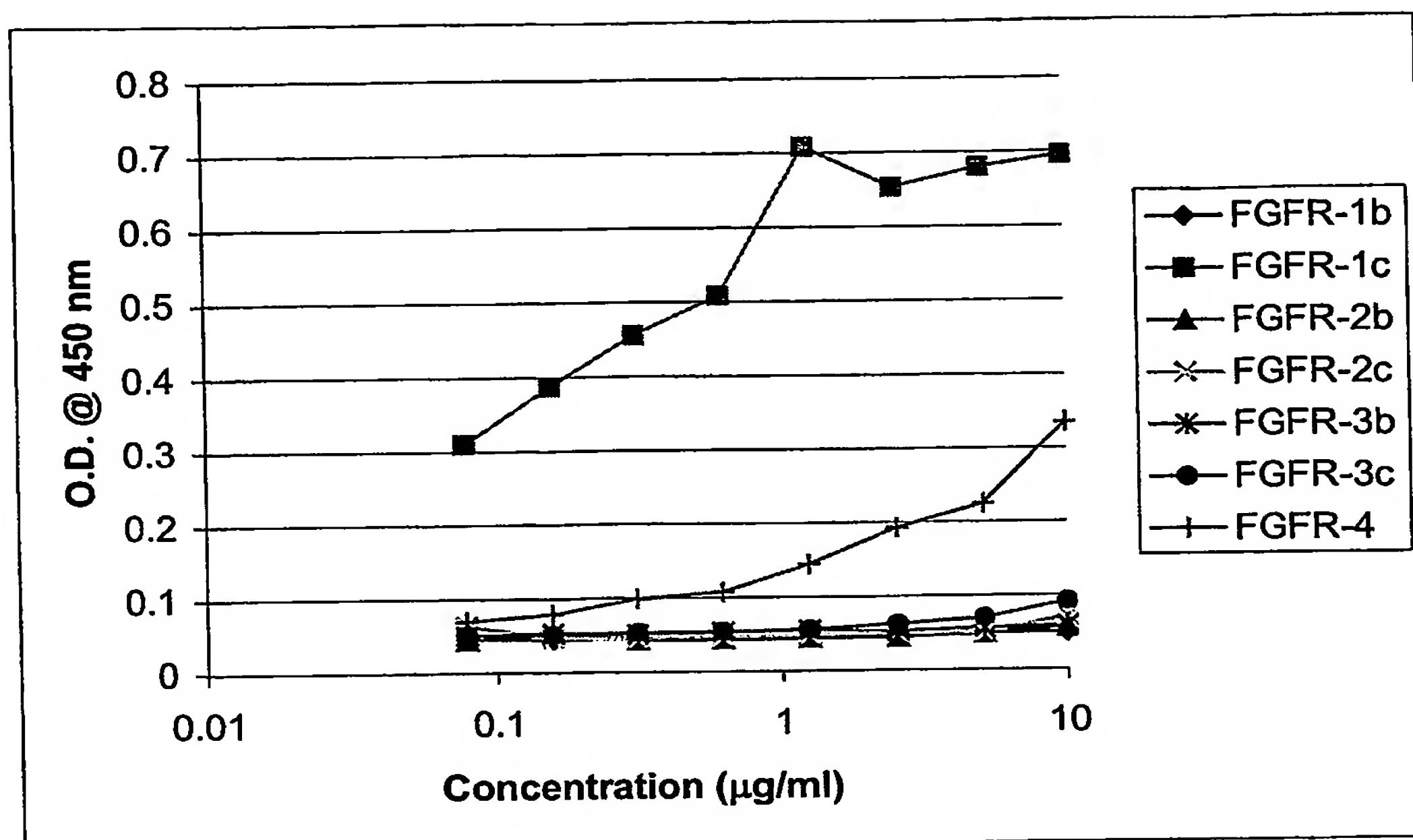


Fig. 21

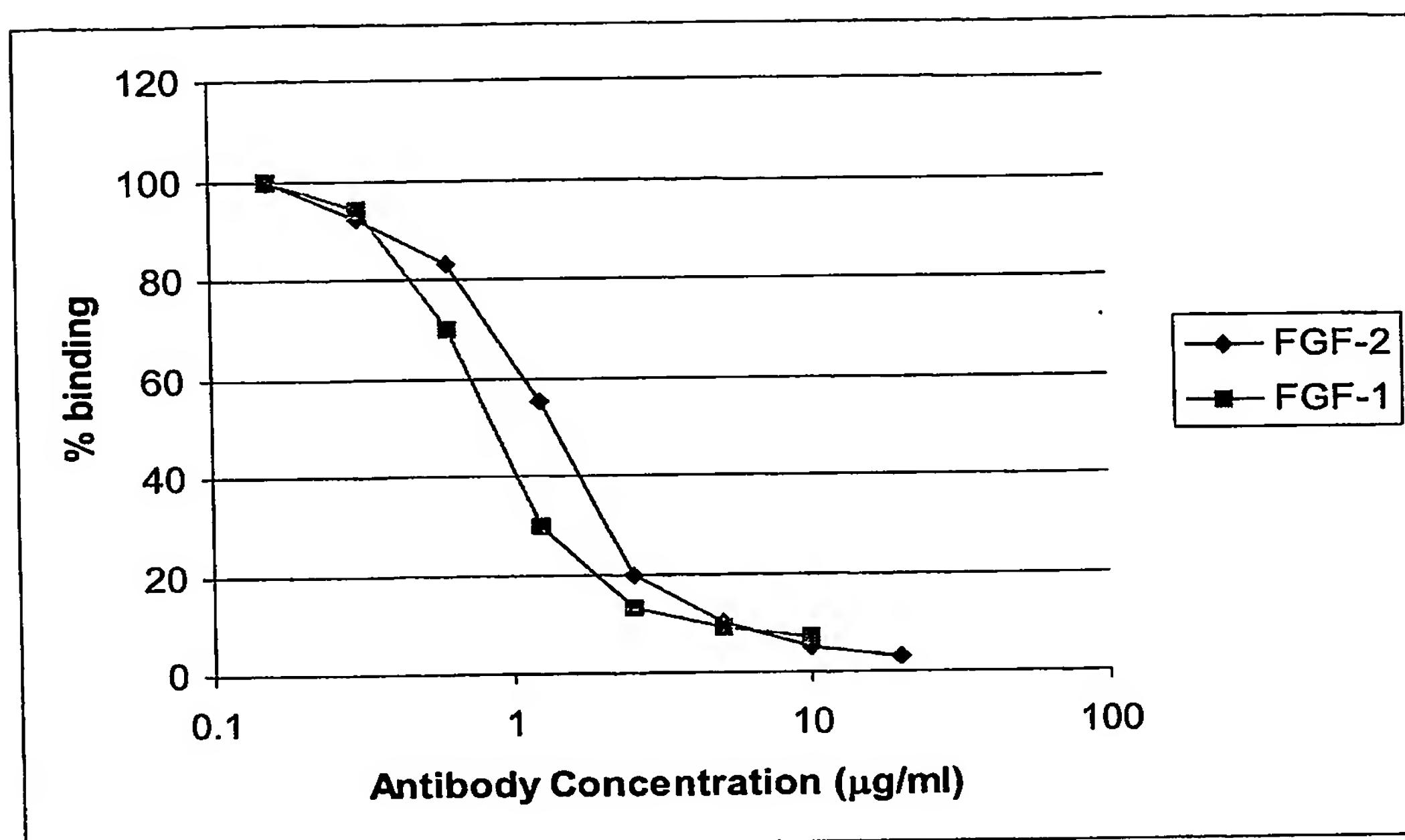


Fig. 22

FGF-2
50 50 - -
(ng/ml)

FR1-A1
- 10 10 -
(μg/ml)

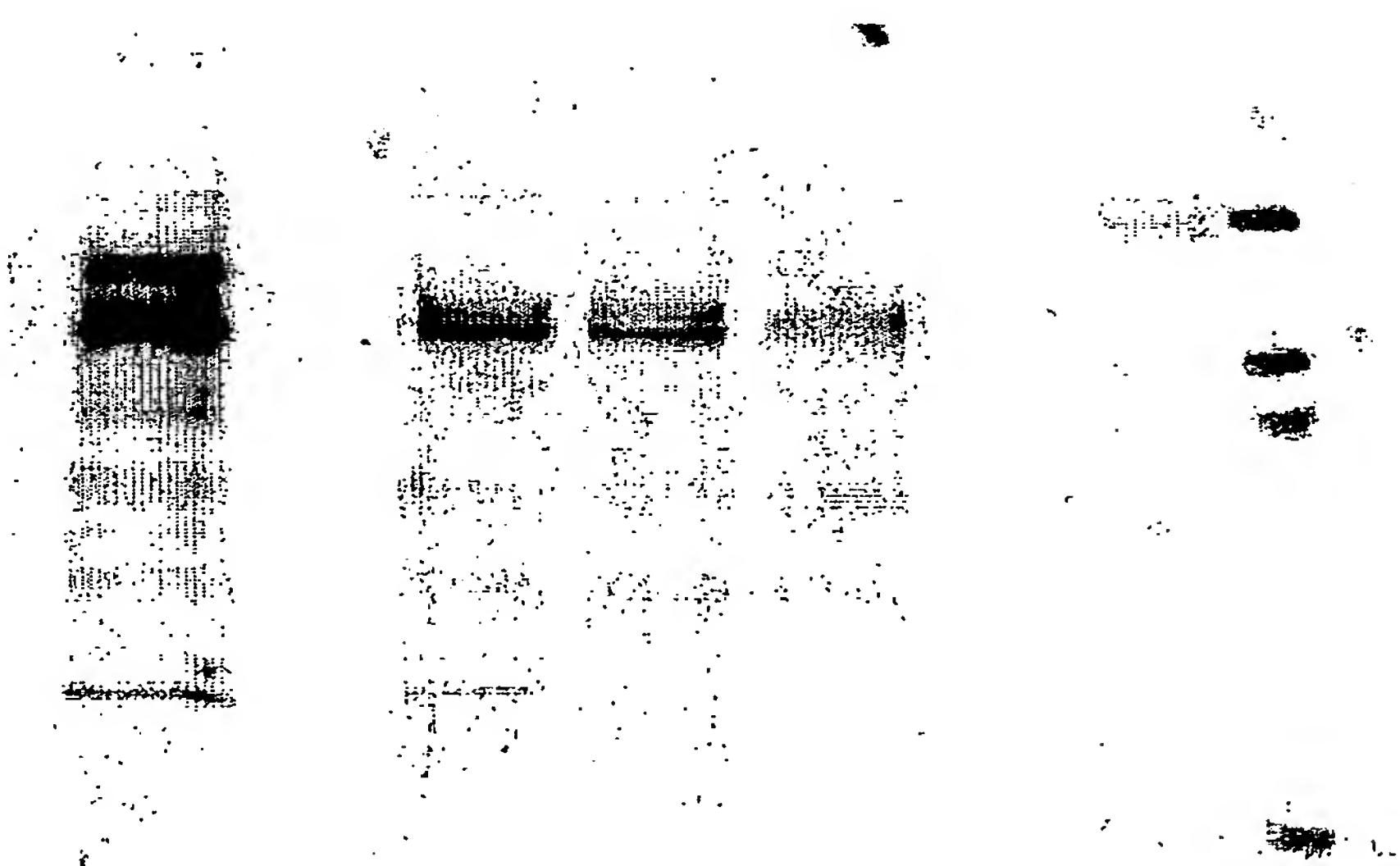


Fig. 23

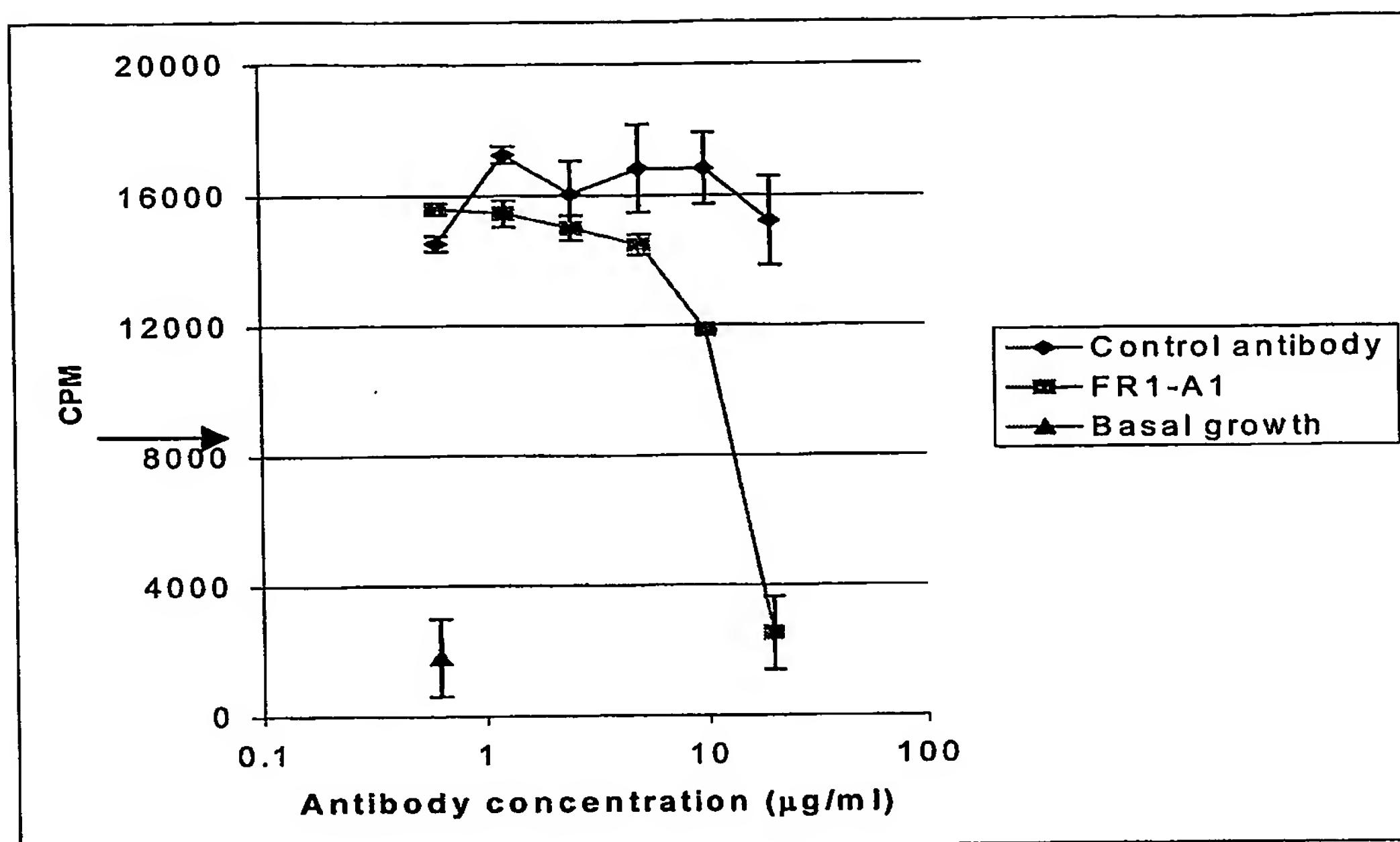


Fig. 24

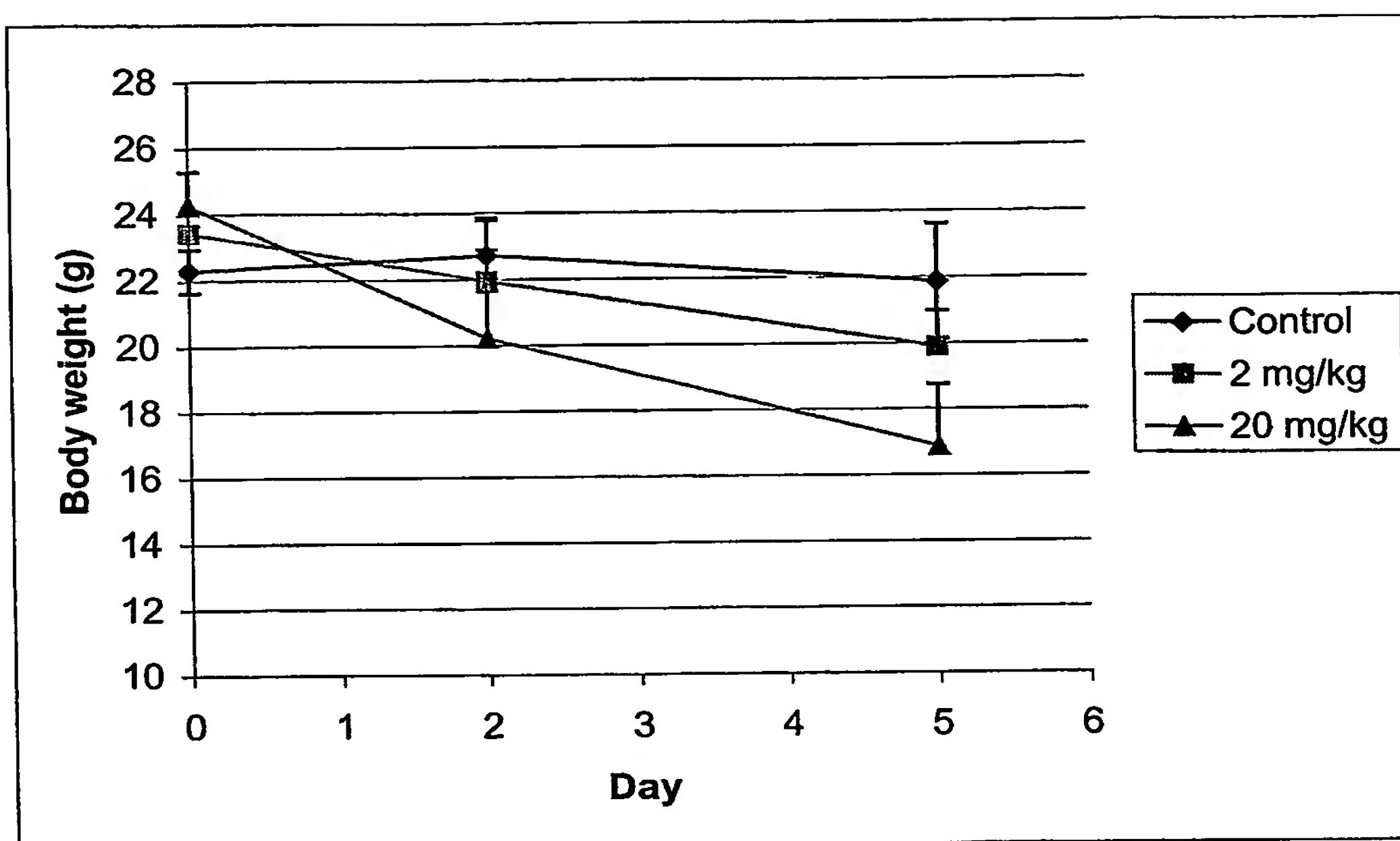


Fig .25

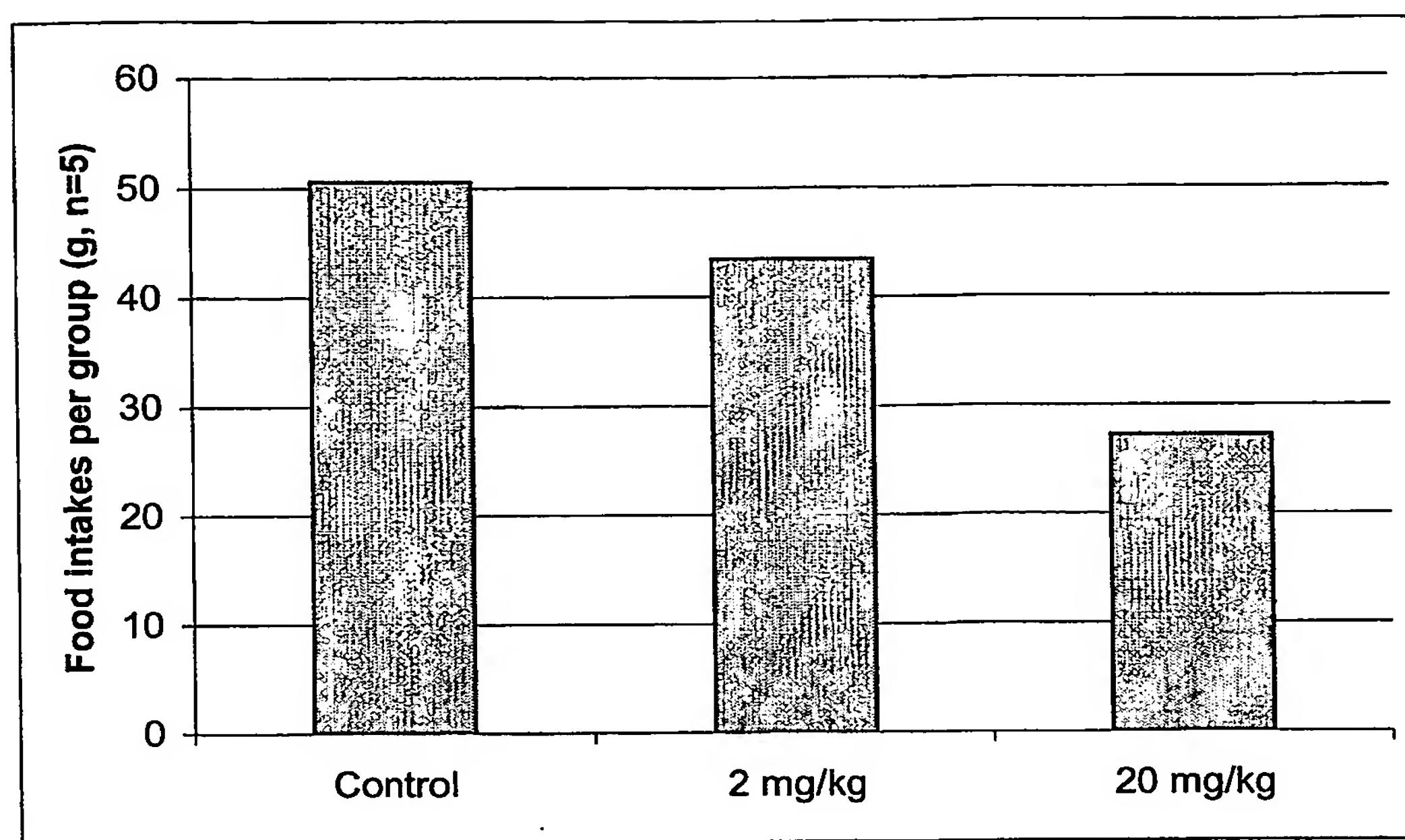


Fig. 26A

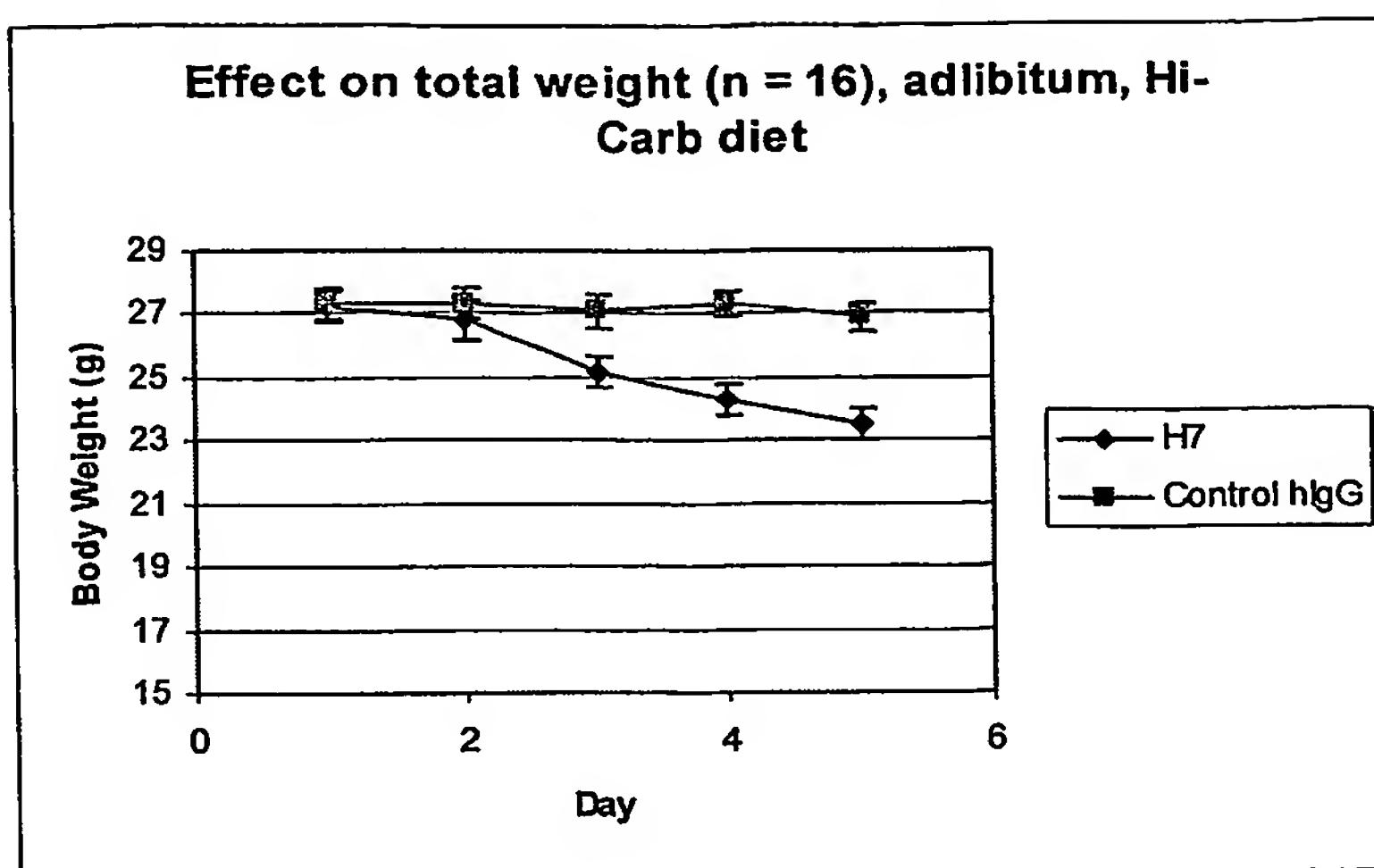


Fig. 26B

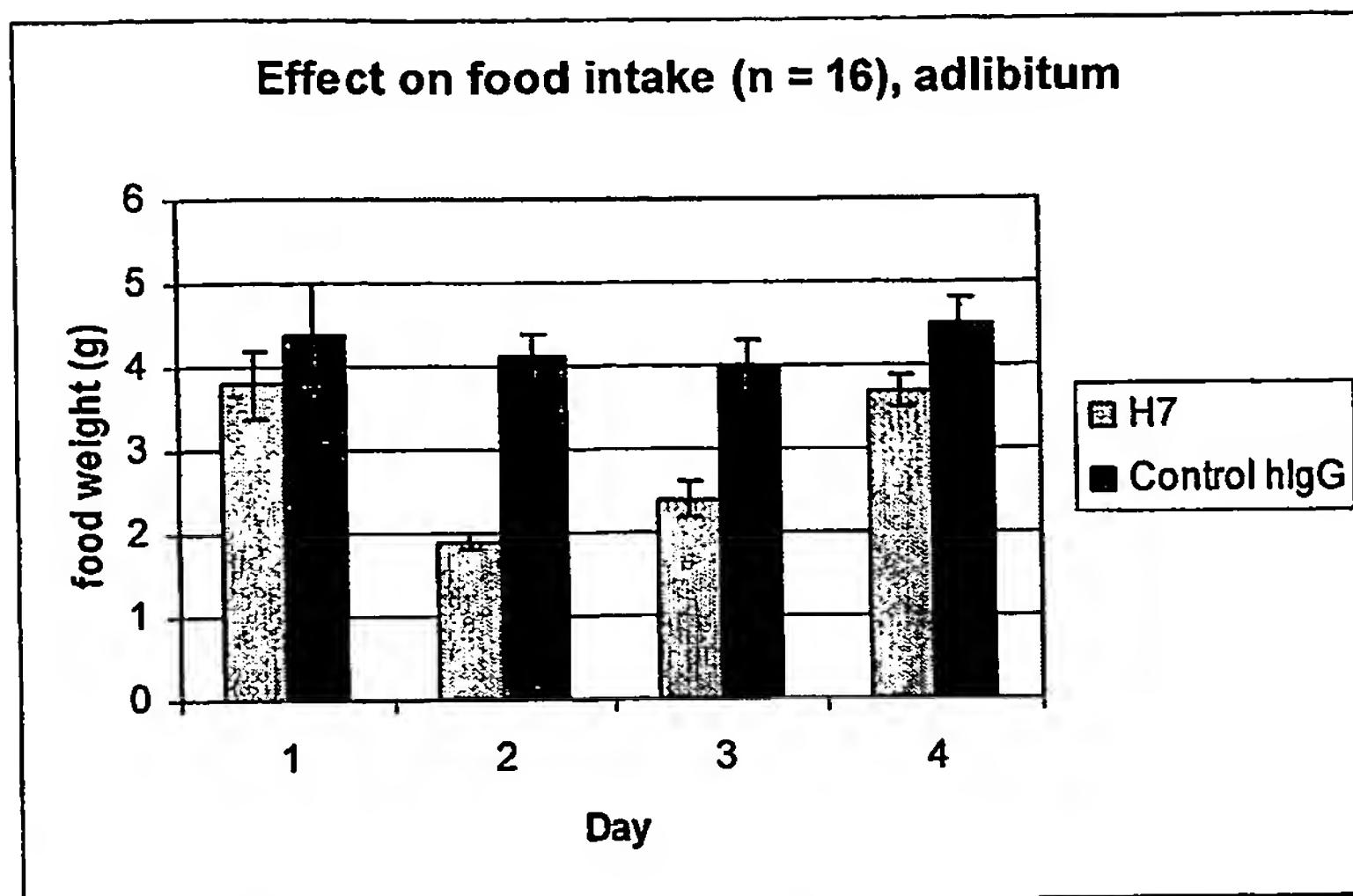


Fig 26C

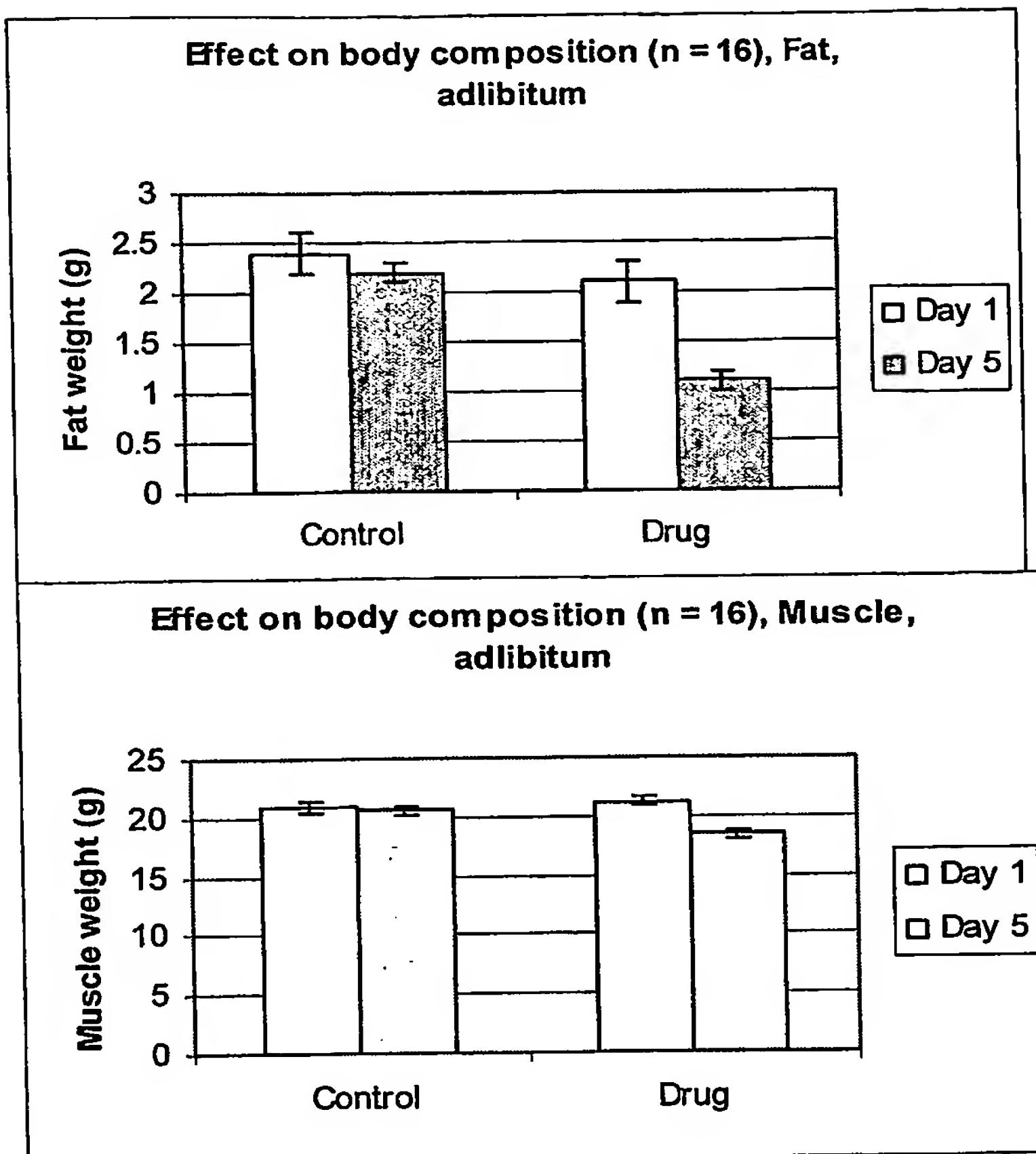


Fig. 26D

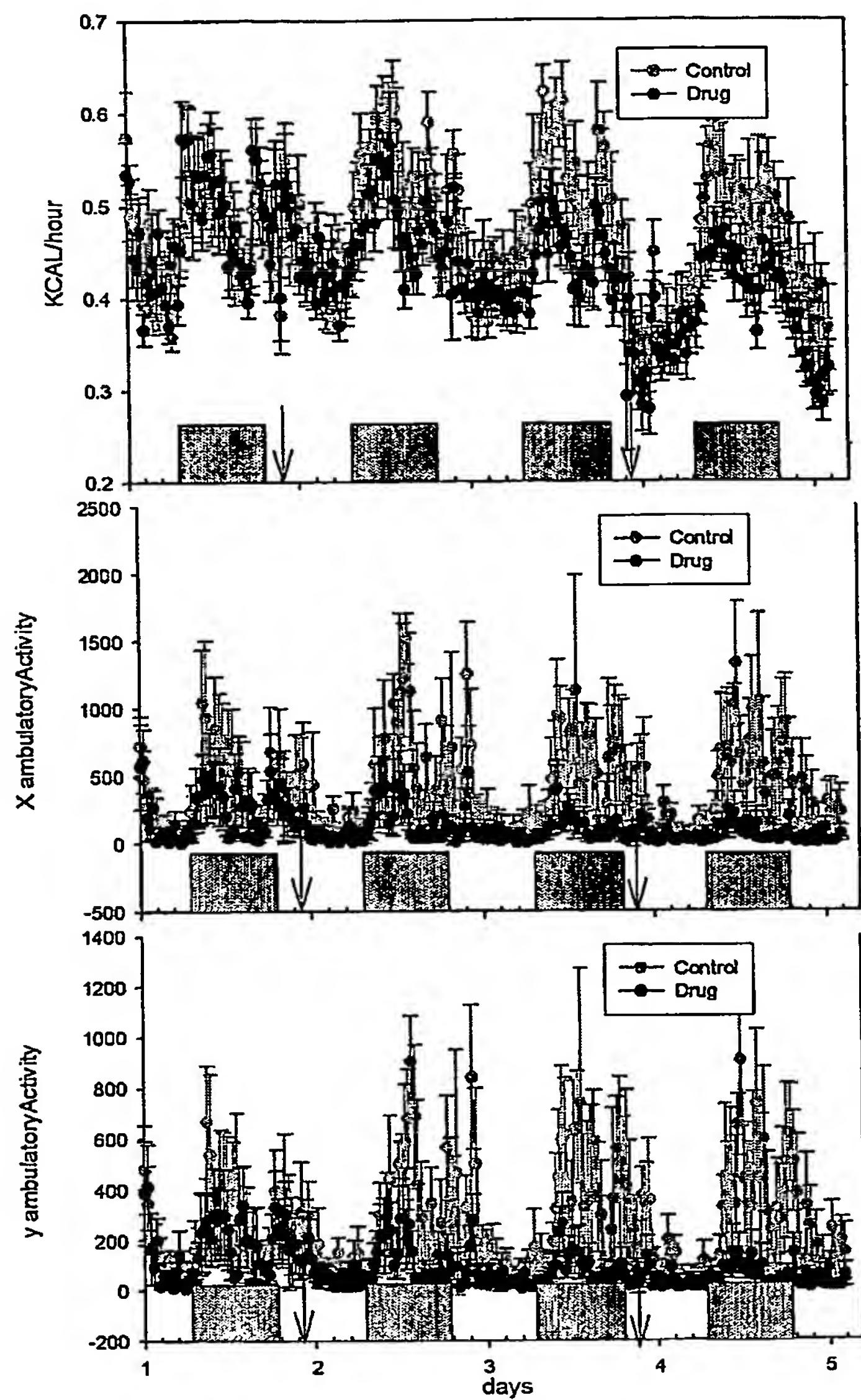


Fig. 26E

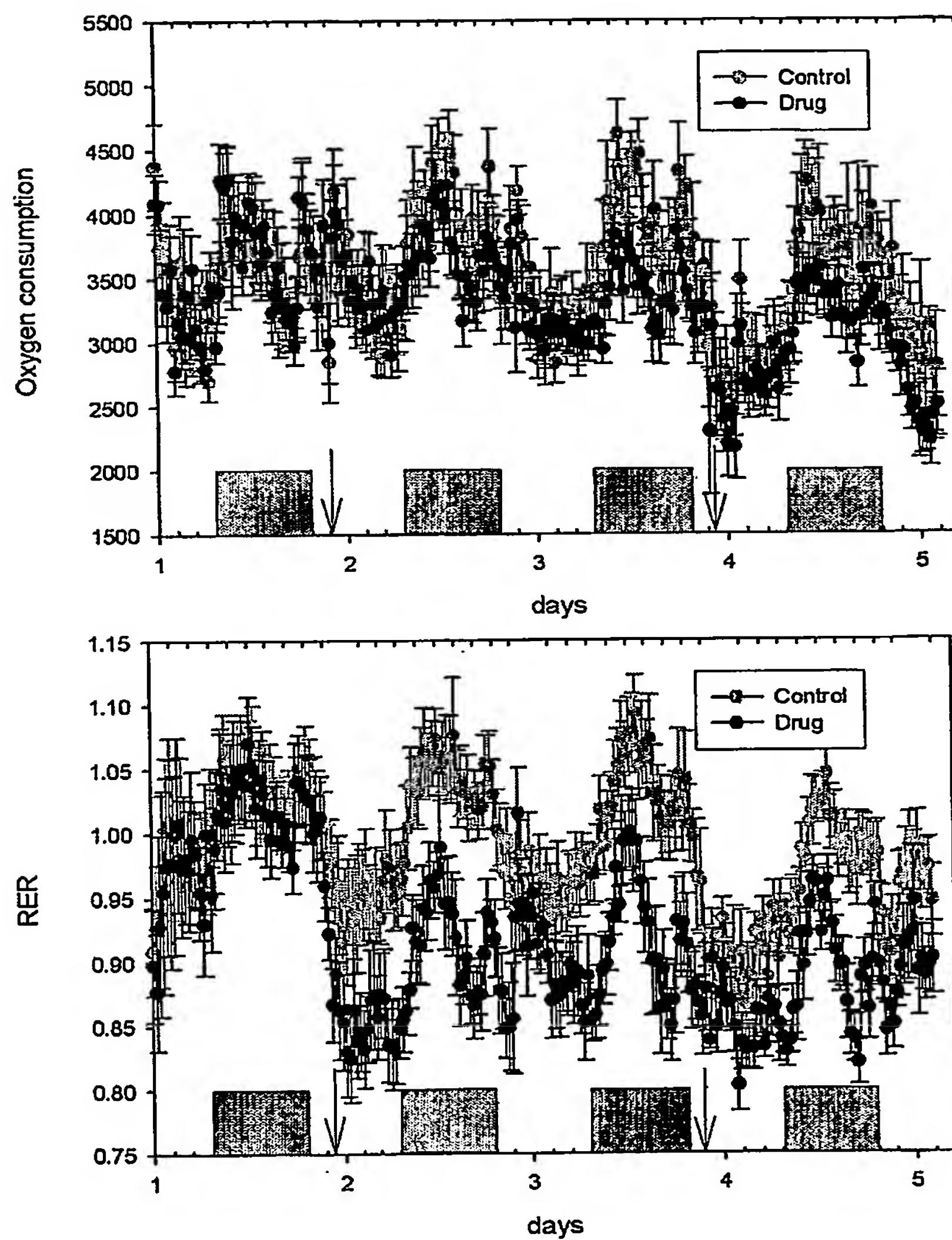


Fig. 27A

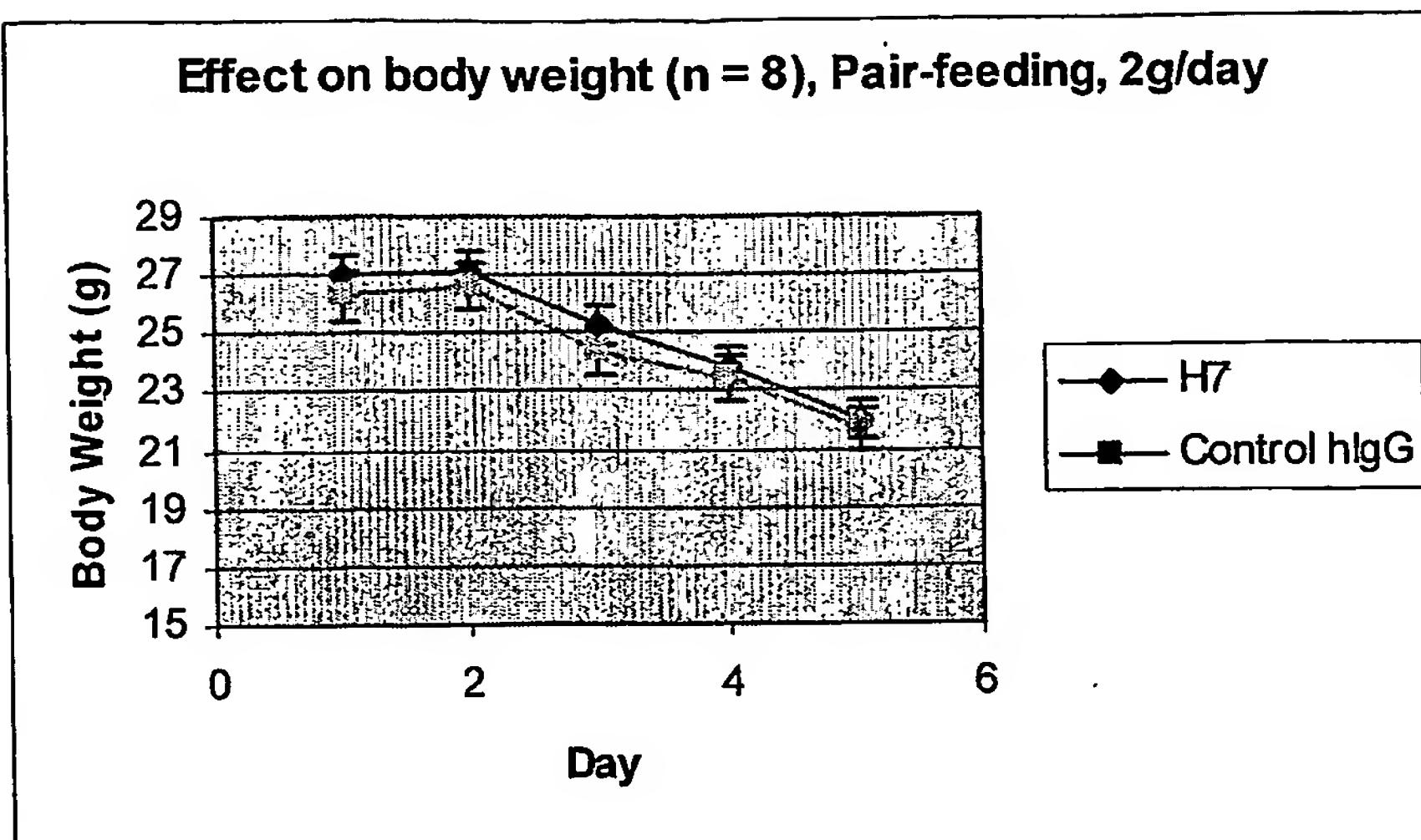


Fig. 27B

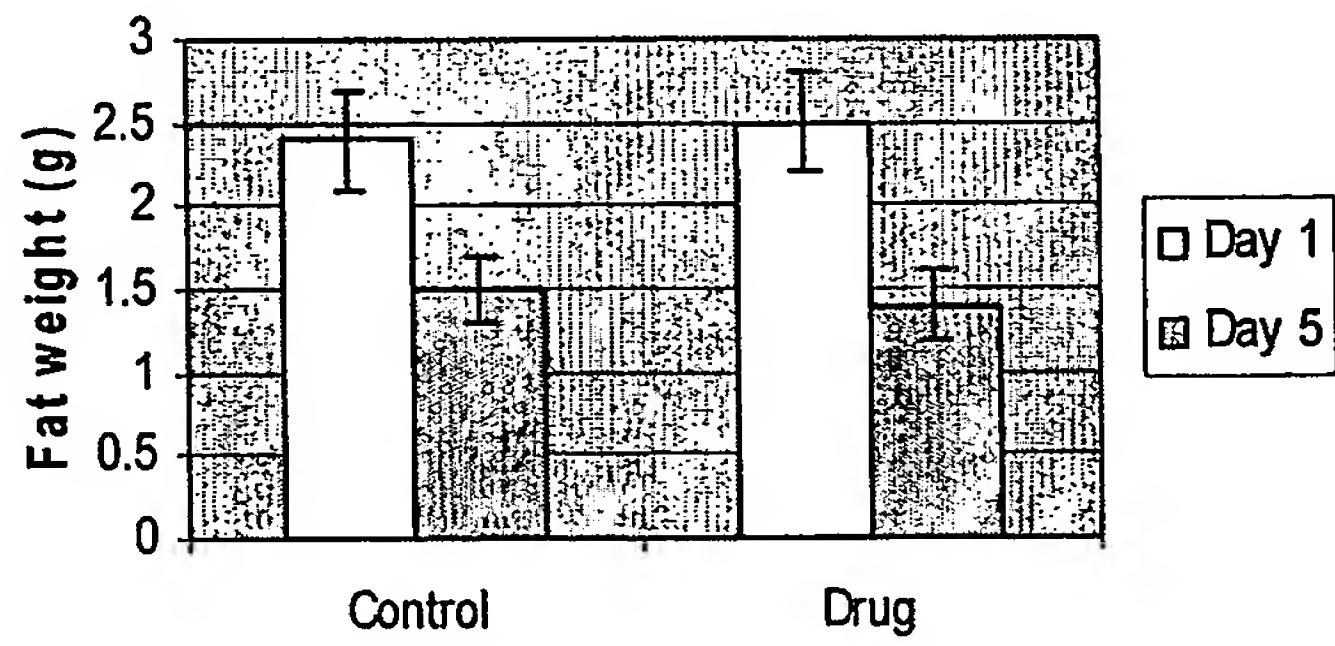
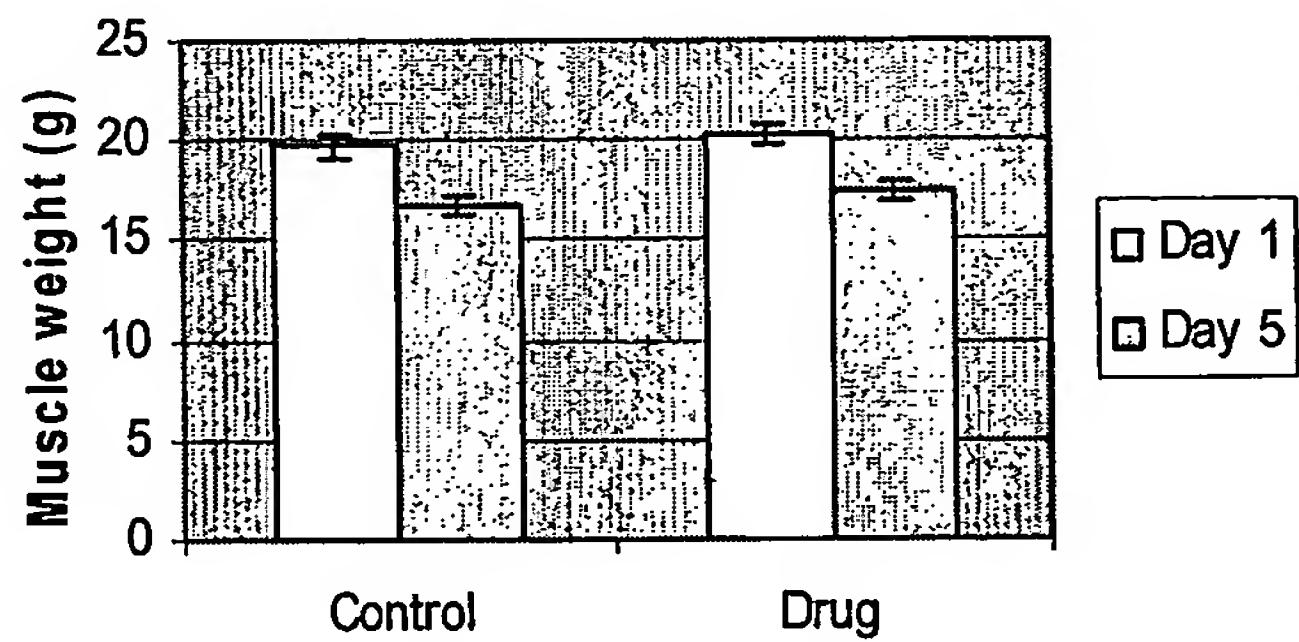
**Effect on body composition (n = 8), Fat weight,
pair-feeding****Effect on body composition (n = 8), Muscle
weight, pair-feeding**

Fig. 27C

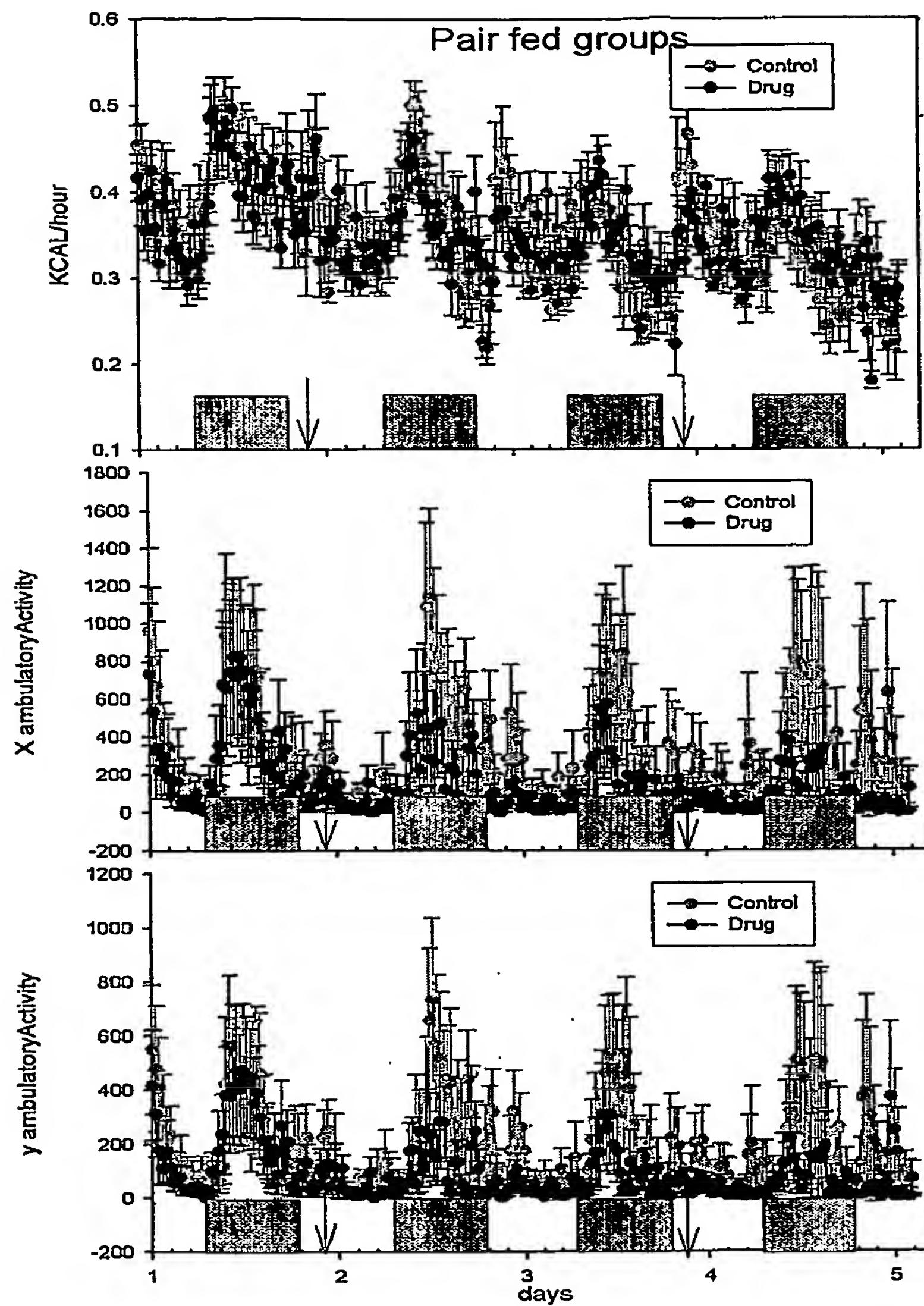


Fig. 27D

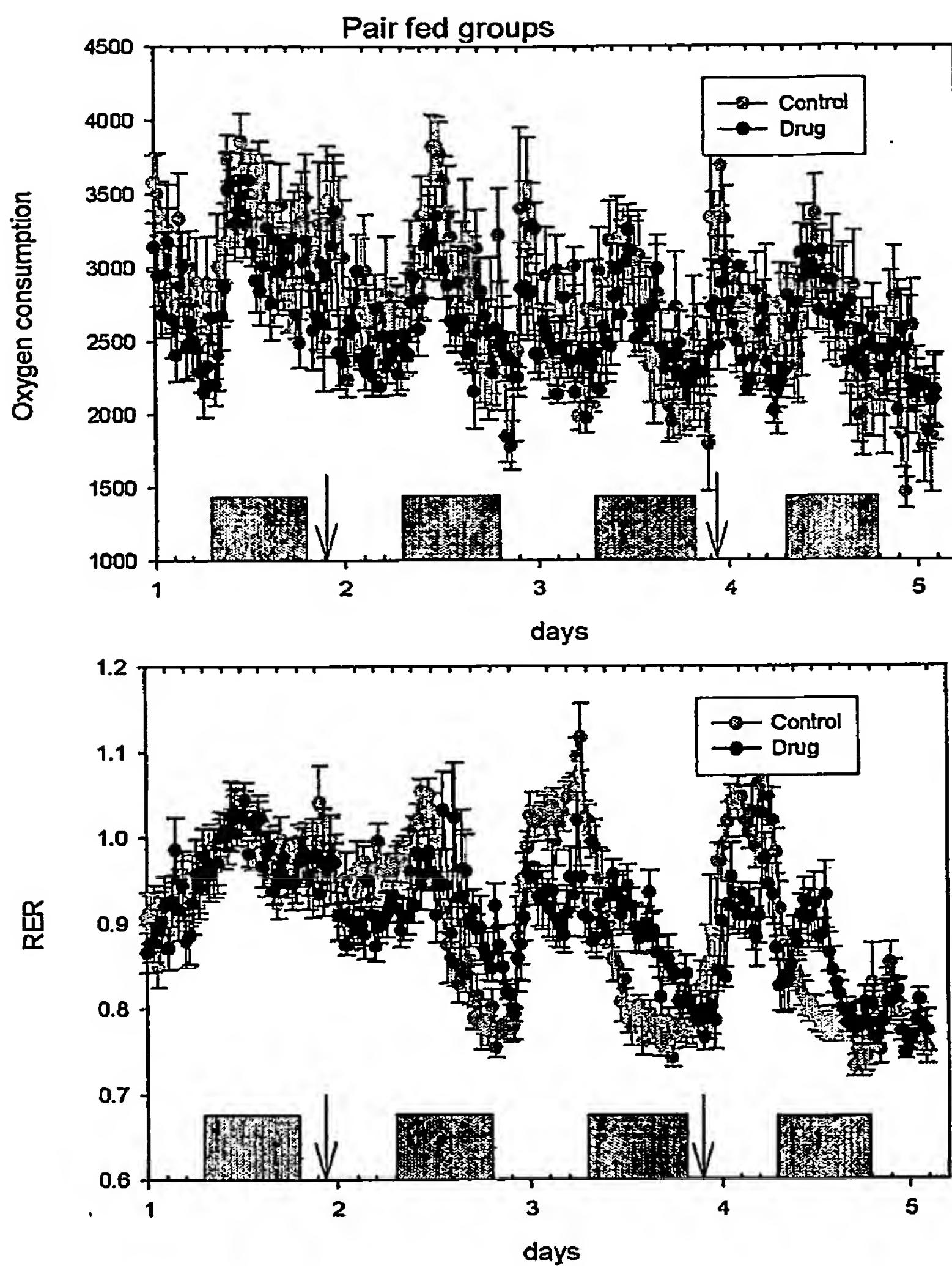


Fig. 28A. FR1-4H antibody variable sequences

Heavy chain variable region sequence (cDNA)
(gamma heavy chain)

CAGGTGCAGCTGGTGGAGTTGGGCCAGGACTGGTGAAGCCTCGGAGAC	50
CCTGTCCTCACCTGCACTGTCTGGTGGCTCCATCAGTAGTTACTACT	100
GGAGCTGGATCCGGCAGCCCCAGGGAAGGGACTGGAGTGGATTGGGTAT	150
ATCTATTACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGT	200
CGCCATATCAGTAGACACGTCCAAGAACCAAGCTCCCTGAAGCTGAGCT	250
CTGTGACCGCCGCGGACACGGCCGTGTATTACTGTGCGAGAGAGTATTAC	300
TATGATAGTAGTGGTTATTACTTTATGCTTTGATATCTGGGGCCAAGG	350
GACCACGGTCACCGTCTCAAGC	372

Heavy chain variable region sequence (amino acid)

QVQLVEFGPGLVKPSETLSLTCTVSGGSISYYWSWIRQPPGKGLEWIGY	50
IYYSGSTNYNPSLKSRSVAISVDTSKNQFSLKLSVTAAADTAVYYCAREYY	100
YDSSGYFYAFDIWGQGTTVTVSS	124

Light chain variable region sequence (cDNA)

CTGCCTGTGCTGACTCAGCCCCCTCAGCGTCTGGACCCCCGGGCAGAG	50
GGTCTCCATCTCTTGTCTGGAAAGCAGCTCCAACATCGGAAGTAATTATG	100
TATACTGGTACCAGCAGCTCCAGGAACGGCCCCAAACTCCTCATCTT	150
AGGAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCAA	200
GTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGCTCCGGTCCGAGGATG	250
AGGCTGATTATTACTGTGCAGCATGGATGACAGCCTGAGTGGTTGGGTG	300
TTCGGCGGAGGGACCAAGCTGACCGTCCTAGGT	333

Light chain variable region sequence (amino acid).
(Lambda light chain)

LPVLTQPPSASGTPGQRVSISCGSSSNIGSNYVYWYQQLPGTAPKLLIF	50
RNNQRPSGVPDFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLSGWV	100
FGGGTKLTVLG	111

Fig. 28B. FR1-4H antibody variable sequence CDRs**CDR amino acid sequences****V_H:**

CDR1	SYYWS
CDR2	YIYYSGSTNYNPSLKS
CDR3	EYYYDSSGYYFYAFDI

V_L:

CDR1	SGSSSNIGSNVY
CDR2	RNNQRPS
CDR3	AAWDDSLSGWV

CDR nucleic acid sequences**V_H:**

CDR1	AGTTACTACTGGAGC
CDR2	TATATCTATTACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGT
CDR3	GAGTATTACTATGATACTAGTAGTGTTATTACTTTATGCTTTGATATC

V_L:

CDR1	TCTGGAAGCAGCTCCAACATCGGAAGTAATTATGTATAC
CDR2	AGGAATAATCAGCGGCCCTCA
CDR3	GCAGCATGGATGACAGCCTGAGTGGTTGGGTG

Fig. 29

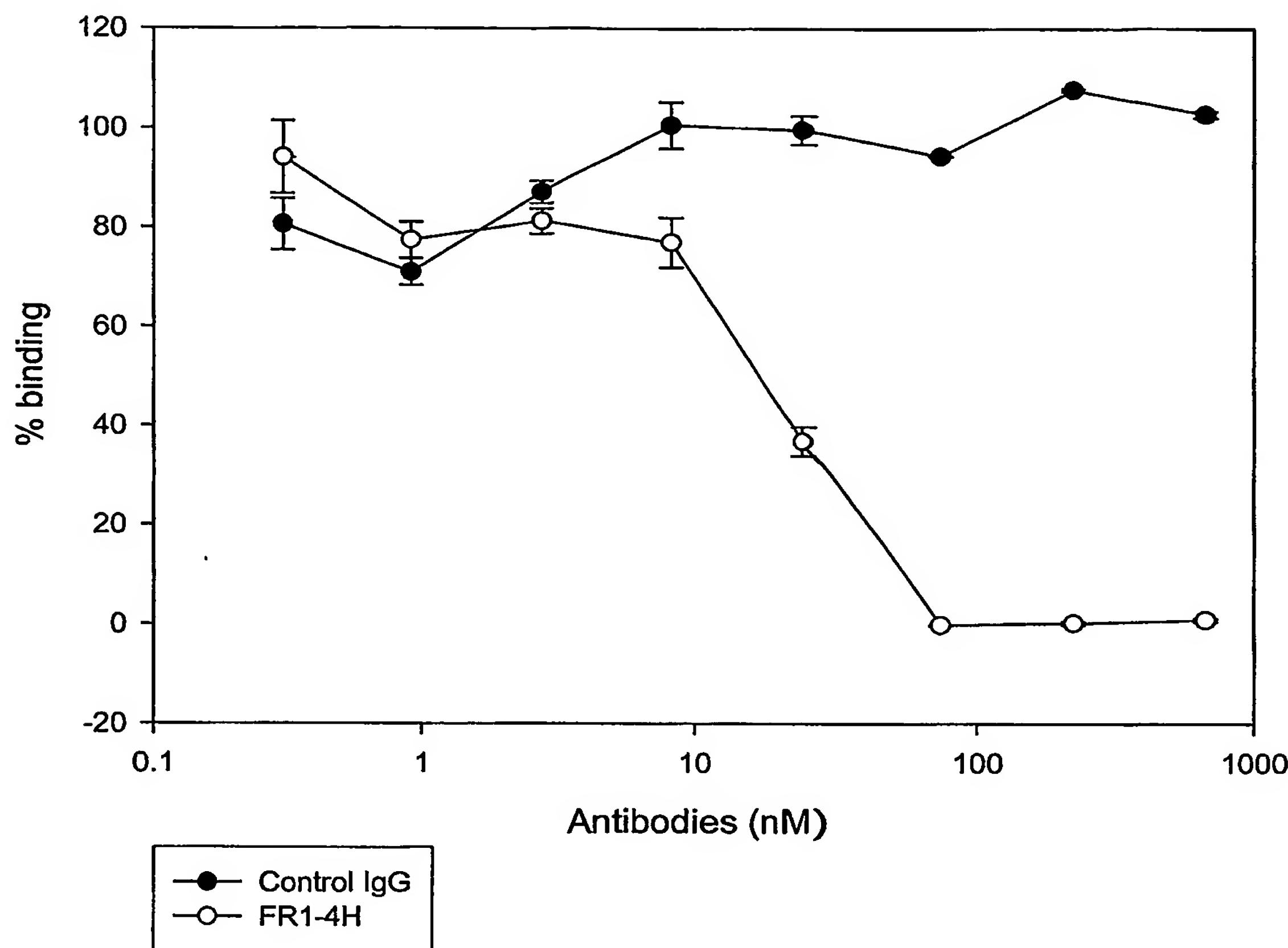
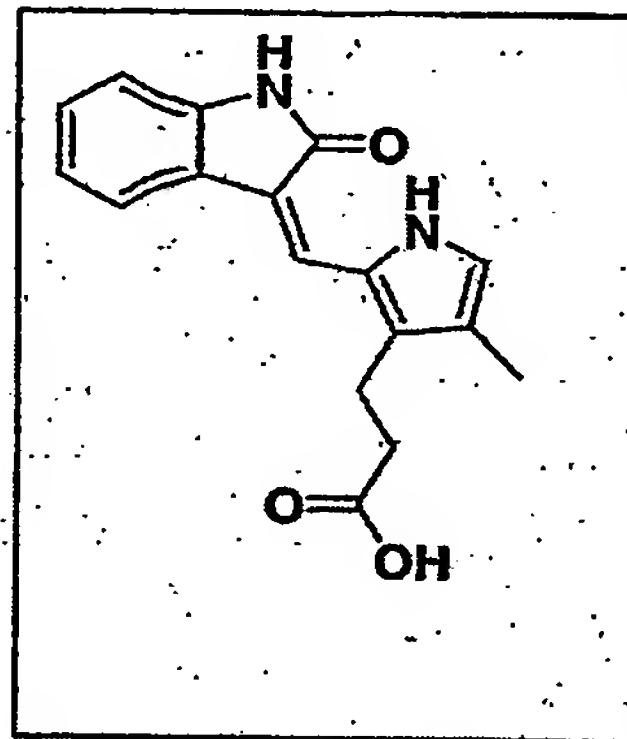
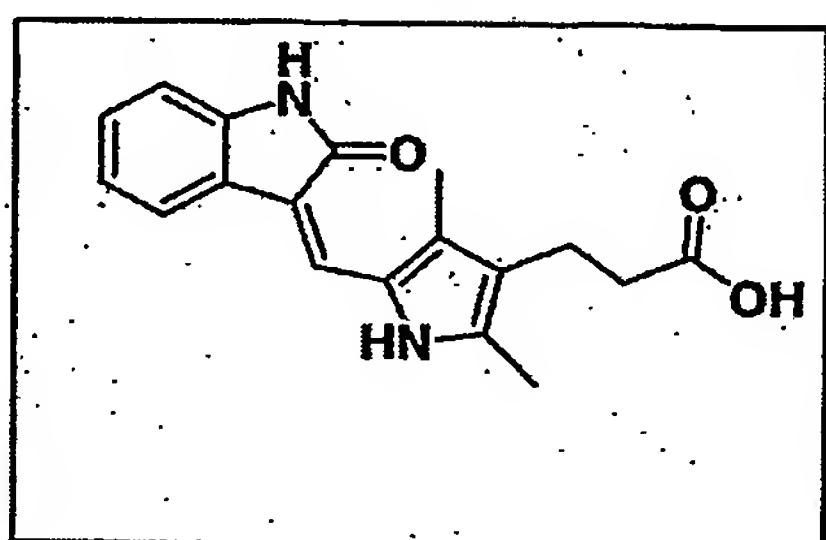
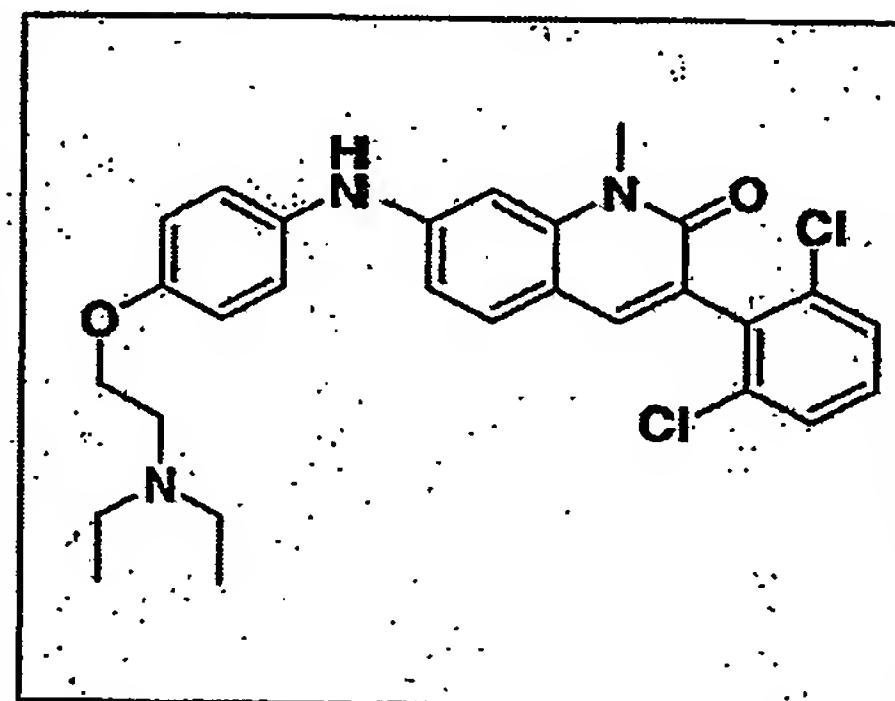
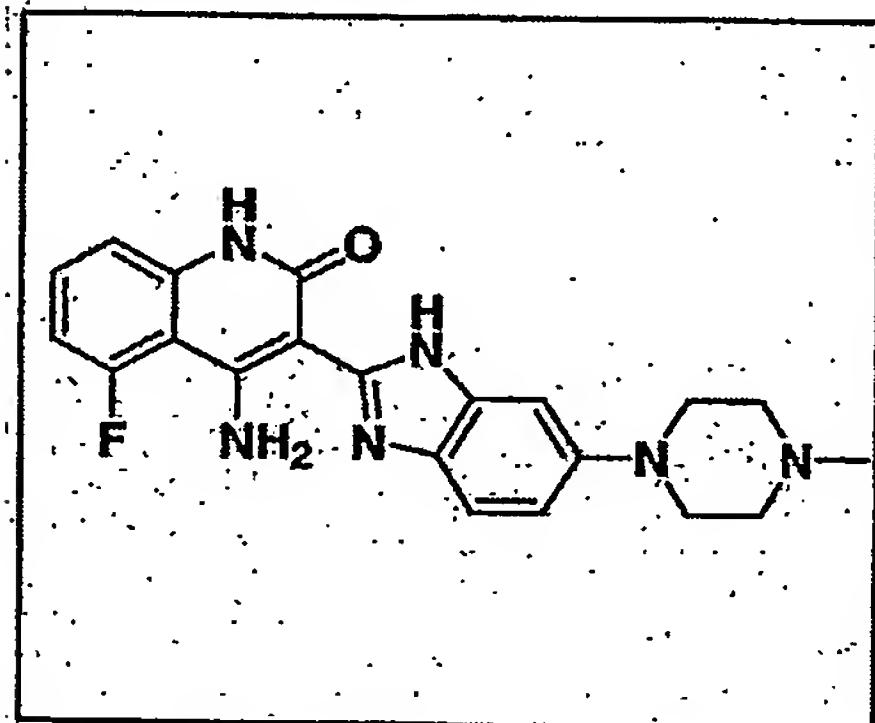


Fig. 30. Examples of FGFR small molecule inhibitors.

Indolinone derivatives:



Quinolinone derivatives:



Pyrimido-pyridine derivatives:

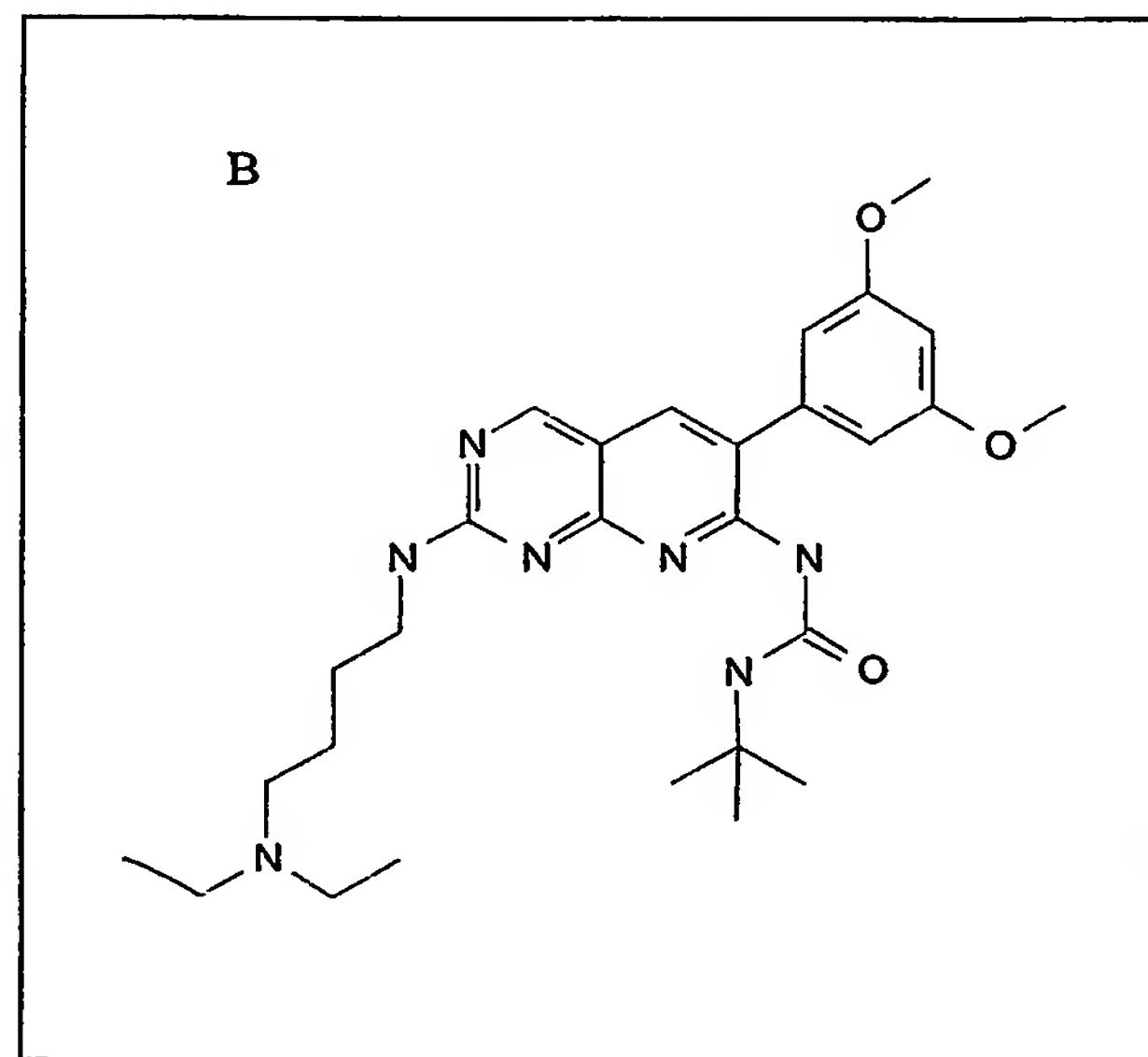
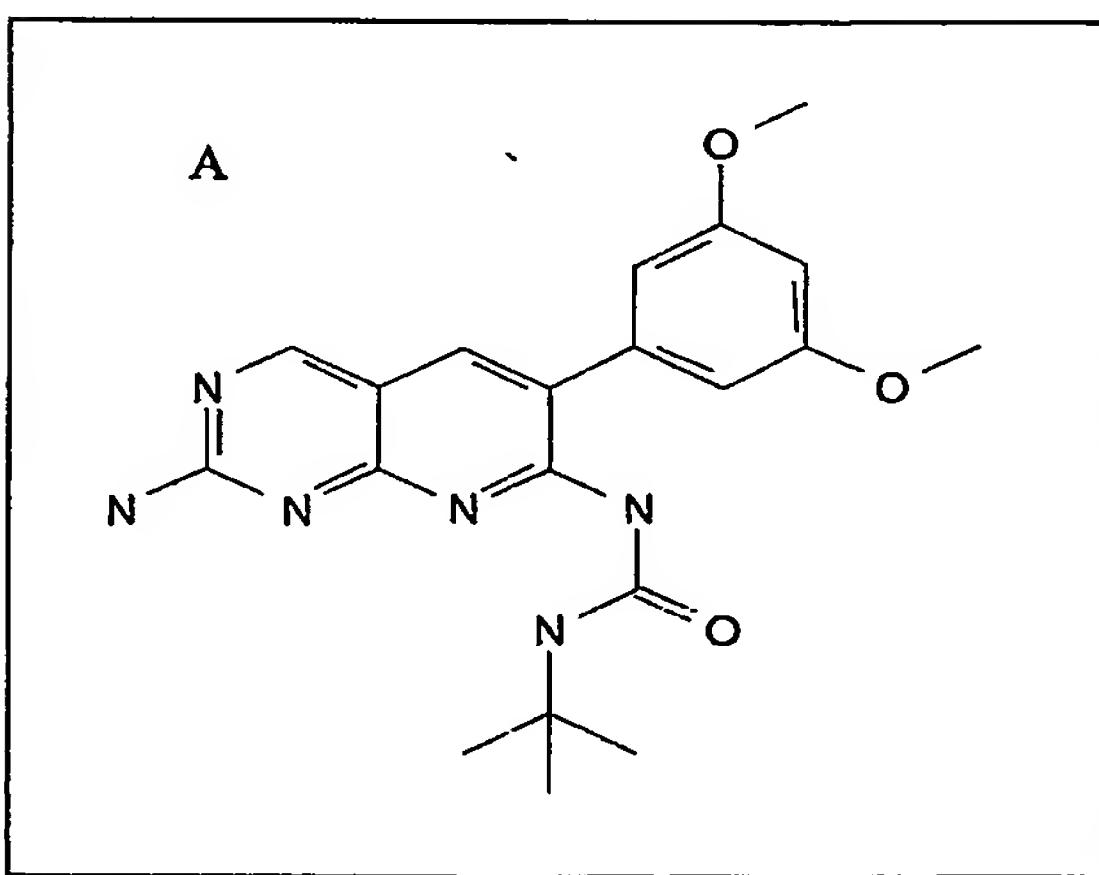


Fig. 31.

FGF	-	5 ng	5 ng	5 ng	5 ng	5 ng	5 ng
Pryimido-pyridines derivative A	-	-	0.5 μ M	0.2 μ M	0.1 μ M	0.05 μ M	0.02 μ M



FGF	-	100 ng	100 ng	100 ng	100 ng
Pryimido-pyridines derivative B	-	-	0.1 μ M	0.03 μ M	0.01 μ M

